Mandooh Gynecology and Obstetrics

GYNECOLOGY

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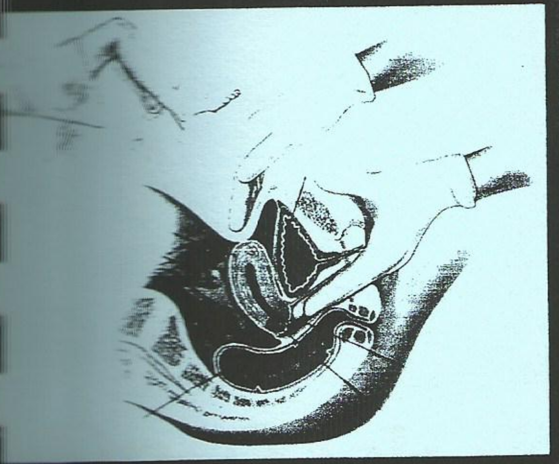


BY

Dr. Mohamed El_Mandooh

Assistant professor of Obstetrics_Gynecology
Ain Shams University

WWW.DR-MANDOOH.COM

Contents

Chapter 1: Basic Science
- Anatomy 1
- Embryology 13
- Physiology 19

Chapter 2: Endocrinology
Puberty 28
Menopause 31
- Amenorrhea 36
Anovulation-PCO 46
- Abormal bleeding 56
- Dysmenorrhea 64

Chapter 3: Infertility
Etiology 68
Assessment 71
Treatment 76
Assisted reporoduction 80

Chapter 4: Contraception
Physiological 83
Mechanical 85
IUCD 86
Hormonal contraception 90
Surgical sterilization 97

Chapter 5: Infection
Vaginal discharge 100
Sexually transmitted disease 102
Vulvovaginitis 107
Cervicitis 110
Pelvic inflammatory disease 114
Chronic granulomatous disease 119

Chapter 1

Basic Science

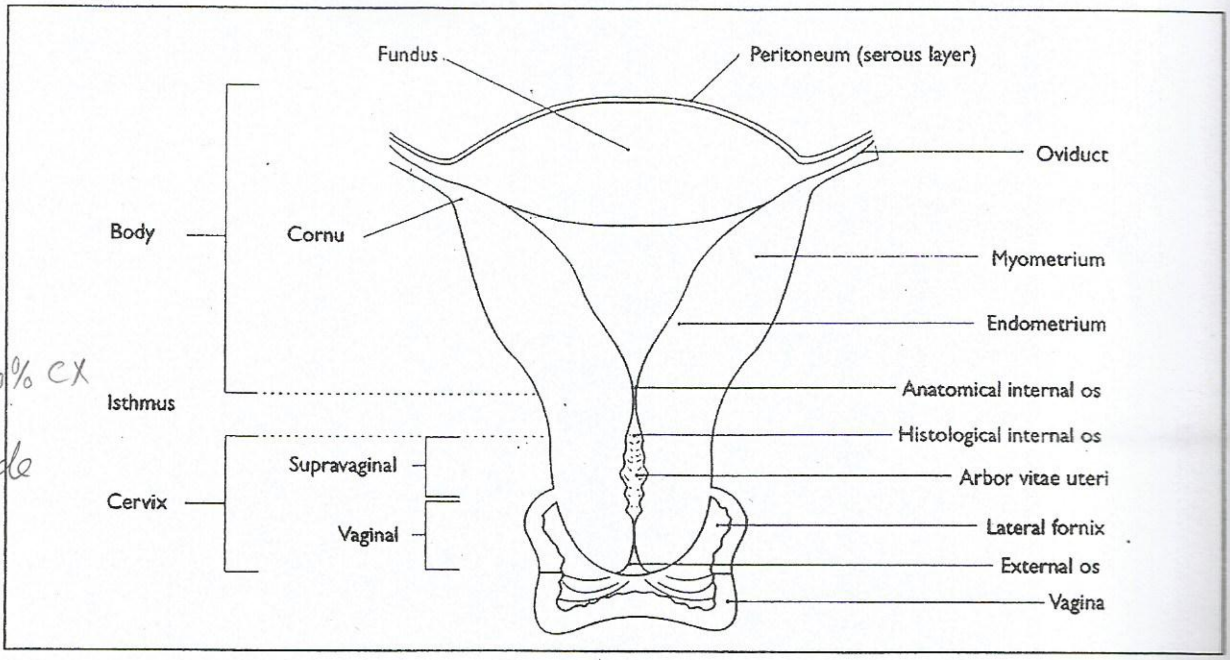
Anatomy

Embryology

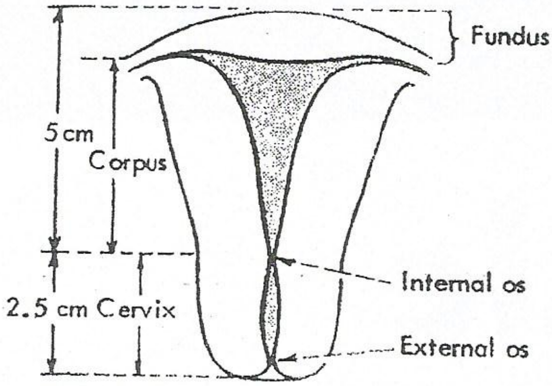
Physiology

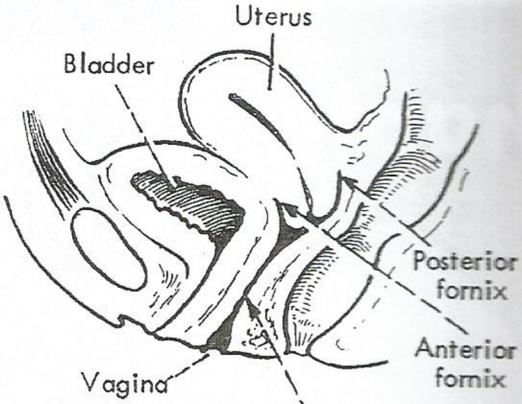
* Uterus = Body + CX

0% — %100 Epithelium
% 100 — %0 muscle
10% CX

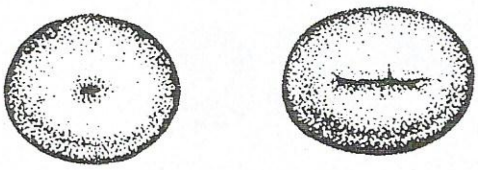


Coronal section of the uterus showing the cavity and the cornual areas.

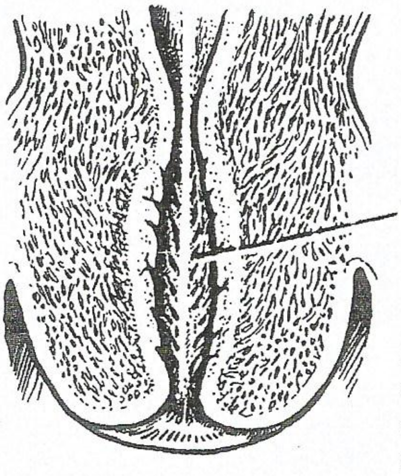




Sagittal Section. Note anterior and posterior walls normally in contact, also anterior and posterior fornices.

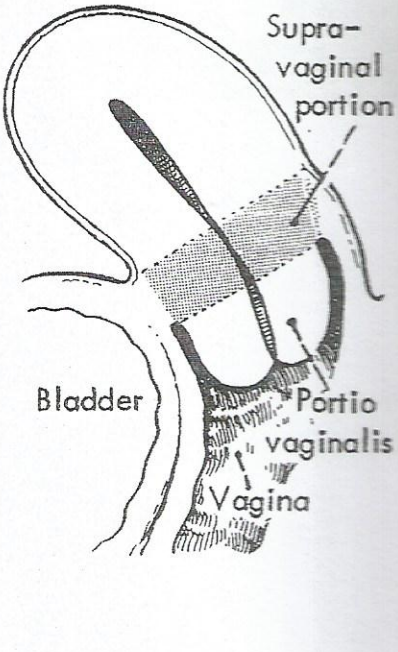


Nulliparous os Parous os



The cervical canal is fusiform and marked by curious folds called the 'arbor vitae'.

The cervix is divided into supra- and infravaginal portions by the attachments of the vagina. The infravaginal part is also called the 'portio vaginalis'.



The site of palpation and massage of uterus is the fundus (The strongest muscle.

Anatomy

Applied anatomy

The myometrium divided into 3 parts: 1- Inner circular:

- Uterus -

▶ **Structure**

- Hollow pear shaped muscular organ
- Dimensions = 3 x 2 x 1″ but (3½ x 2½ x 1½ in multi-gravida)
- Weight = 50 gm but (70–80 gm in multi-gravida)

▶ **Parts**

1- Body (corpus uteri)

- □ Upper ⅔ → 2 inches
- □ Junction with tubes is *cornu*, part above insertion of tubes is *fundus*

☆ **Peritoneum** ⇨ adherent, covers it completely

- *anterior*: uterovesical pouch (between bladder & uterus)
- *posterior*: Douglas pouch (between rectum & uterus)

☆ **Myometrium** ⇨

. *Outer longitudinal*....modified as pace maker of the uterus (modifies as syncytium → site: near the Rt cornu)
. *Inner circular*.........modified as sphincters in 3 sites (① tubal opening → prevent menstrual regurgitation; ② internal os;)
. *Middle oblique* ✓ (the main.)....makes 8 shaped figures around vessels → To prevent PPH (Post Partum Hge).

☆ **Endometrium** ⇨

. Columnar epithelium (partially ciliated) → for sperm transport.
. Glands (simple tubular), stroma & blood vessels
. Sensitive to E & P cyclic changes (*endometrial cycle*)

2- Cervix

- □ Lower ⅓ → 1 inch
- □ Peritoneum → cover it only posteriorly (by the end of preg.: cervical ripening must occur and this is the funct. of false lab. pain.)
- □ Muscle layer → mainly formed of fibrous tissue (ms = 10% only) (→ To be able to support the baby for 9 month.)
- □ Cervical canal → fusiform with ↷

☆ **2 os** internal = 3–4 mm ¤

external = rounded, becomes slit shape in MP ¤ (→ if rounded in MP → all delivery by CS.)

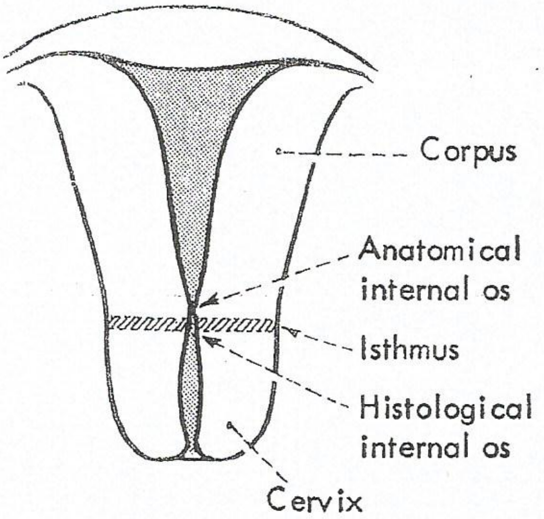
☆ **2 Parts**

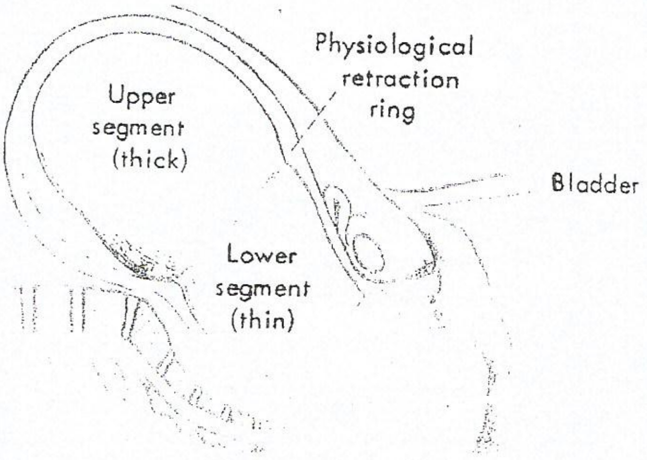
- Part projecting in vag. ⇨ *portio vaginalis* (lined by st.sq.epith.= *ectocervix*)
- Part above vagina ⇨ *supravaginal part* (lined by colum. epith = endocervix) (Cervical canal):
  its mucosa is thrown into folds into which racemose glands open (→ Arbor vitae.)

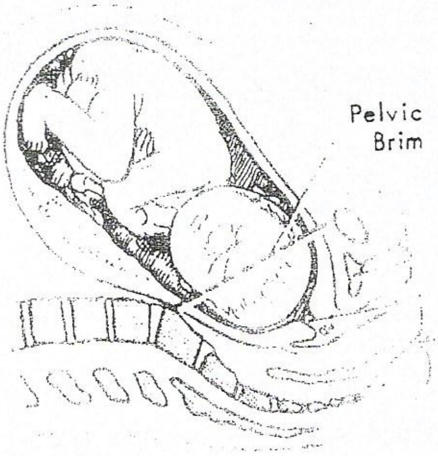
☆ **2 junctions** (Transition (Transformation) Zone → site of start for Cancer CX.)

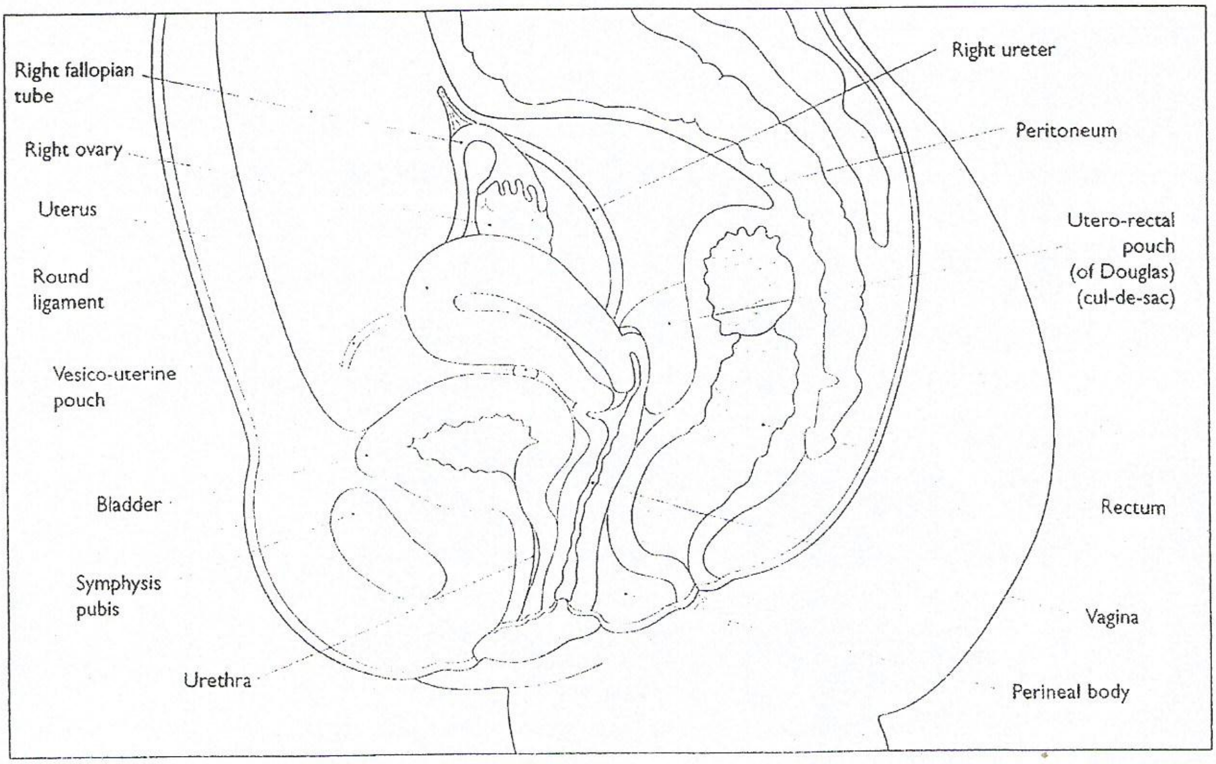
- Squamocolumnar junction (TZ) → between *ectocervix* & *endocervix*
- Histological internal os → between *endocervix* & *endometrium*

e) preg: site of Cx, int. os don't change.









Sagittal section of the pelvis, with the woman in the erect position.

Anatomically: like Cx → weak muscle → for capacitation of fetus during lab.
→ Histologically: like endometrium → covers fetus during preg.

3- Isthmus

- □ 3–5 mm
- □ Between **A**natomical internal os above and **H**istological internal os below
- □ Covered by loose peritoneum → landmark for site of lower segment CS.
- □ In pregnancy forms → the lower uterine segment (10cm)
- □ It differs from the upper segment in ¤

	Upper segment	Lower segment
Peritoneum	Adherent	Loose
Muscle	Thick (3 layers)	Thin (2 layers)
Decidua	Well developed	Less developed
Membranes	Firmly adherent	Loosely adherent
Action	Active in labor (contracts & retracts)	Passive ¤ (dilates & stretches)

- **Physiological retraction ring**

  It is a groove between the thick UUS & thin LUS below the symphysis pubis. Normally it is not *seen* or *palpable*

♠ ***Blood supply of uterus***

❶ uterine artery ✓.......branch from internal iliac artery (ant division)
❷ ovarian artery.........branch from aorta (at L_2)

♠ ***Relation bet. body & cx*** ☞

	Corpus	Cervix
Intrauterine life	1	5
Infantile	1	2
Prepubertal	1	1
* Adult ✓	**2**	**1**
Menopause	Corpus shrinks > cervix	

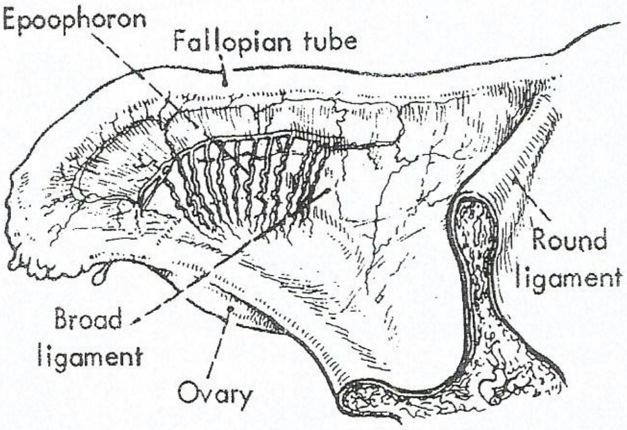
▸ **Normal position of the genital system** AVF

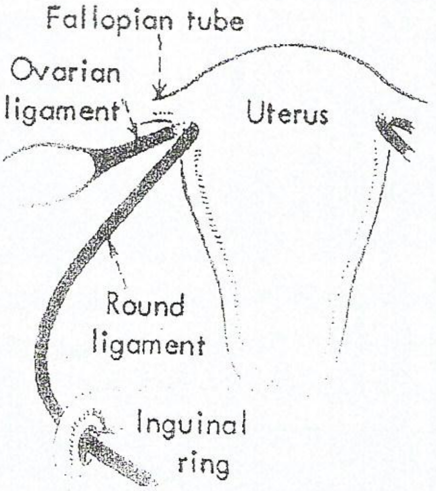
☆ AnteVersion ⇨ whole uterus is inclined forward on vaginal axis by **90°**
↘due to tension between uterosacral & round ligament ¤ شد الرحم لورا شد الرحم لأدام
☆ AnteFlexion ⇨ the body is bent forwards on the cervix by **160-170°**
↘due to the tone of the uterine muscles ¤ → Tone of ant wall > Post wall.

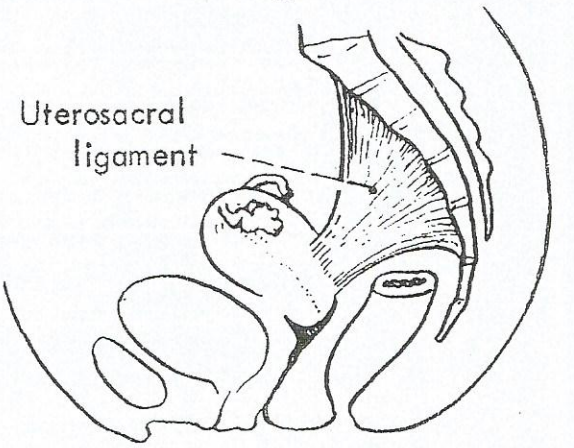
- In 20 % of females the uterus may be ***Normally*** retroverted → RVF

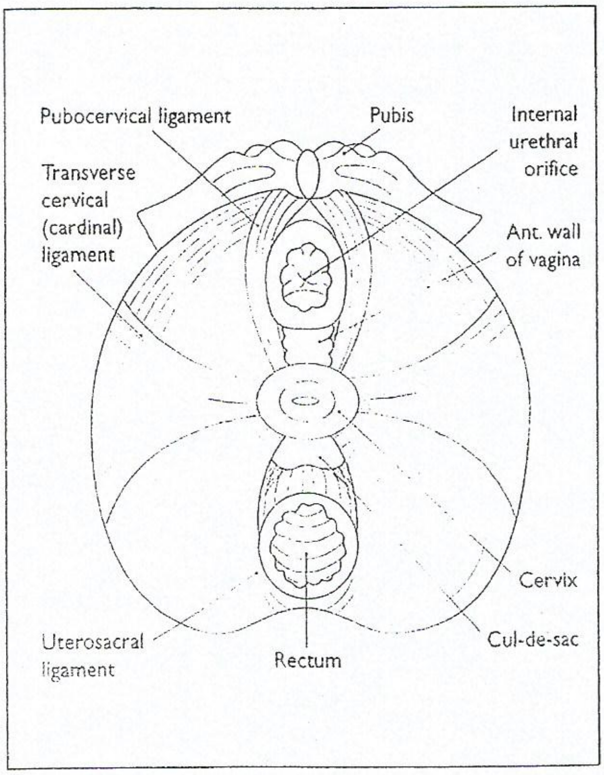
☆ External os lies normally at / above the level of the *ischial spines*
☆ Vagina is directed upwards & backwards forming **45-60°** with horizon

LIGAMENTS OF THE UTERUS

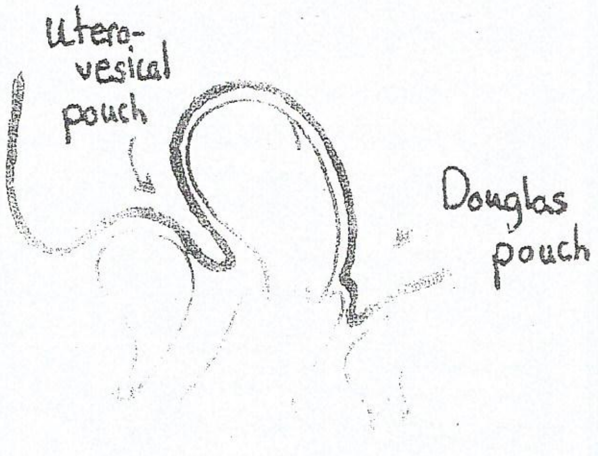


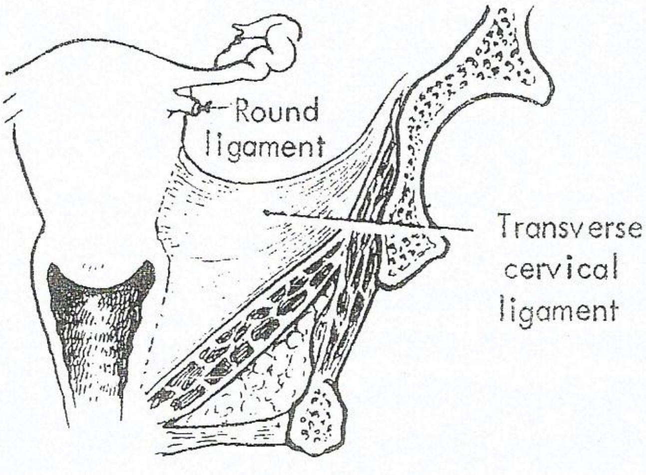


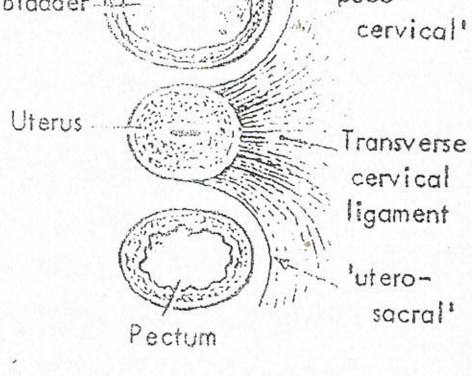




The 'ligaments' of the cervix.







structures attached to Cornu: Tube, Round lig, ovarian lig.

▶ **Supports of the uterus** ✍

- AVF position
- Peritoneal attachment
- Position of the surrounding viscera
- ✓✓ **UTERINE LIGAMENTS (TRUE ONLY)** ¤ ↷ + **LEVATOR ANI** ¤

▶ **Uterine ligaments**

1- *Corporal* (false)

↳ distensible body.

A] Broad ligament

- Fold of peritoneum between lateral uterine border & lateral pelvic wall
- Contents (all are present in loose CT; the parametrium) Φ → CT strong between the 2 leaflets of Broad lig.
  - Upper border: (*medially* → F.tube, *laterally* → infundibulopelvic lig.)
  - Uterine & ovarian vessels
  - Vestigial remnants (epoophron, paroophron, Gartner duct) بواقي اراجيل

B] Round ligament

Both originates from gubernaculum

- From uterine cornu through inguinal canal to insert in *labia majora*
- Raises a ridge on the anterior (inferior) layer of broad ligament ¤
- Important to maintain anteversion
- Supplied by Sampson a. (from ovarian a.) & br. from inferior epigastric a.
  ↳ inside Round lig.

C] Ovarian ligament → from uterine cornu to ovary

2- *Cervical* (true)

↳ fixed cx

A] Anteriorly ➡ **Pubo-cervical lig.** (pubo-cervico-vesical fascia)

B] Laterally ➡ **Mackenrodt lig., cardinal lig., transverse cx lig.**

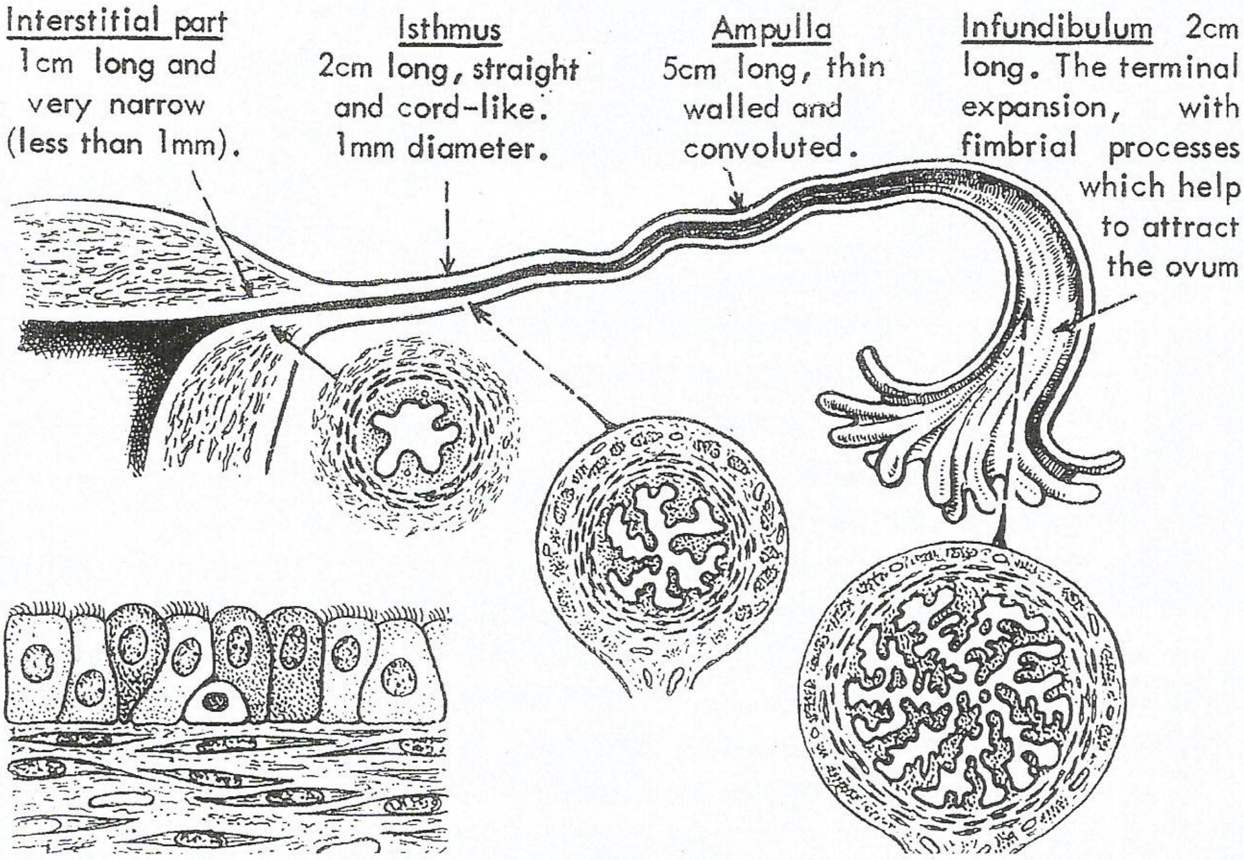
- Strong, fan shaped ligament
- From lateral part of cx & upper part of vag to lat. pelvic wall (*white line*) ¤
- The ureter passes through it (in the ureteric canal) ¤
- It forms the base of the broad ligament
- Provides passage for uterine lig.

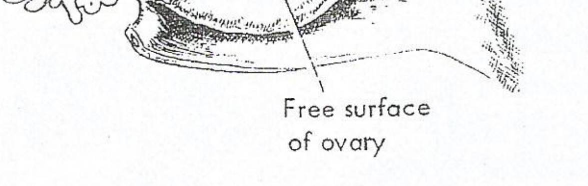
C] Posteriorly ➡ **uterosacral lig.**

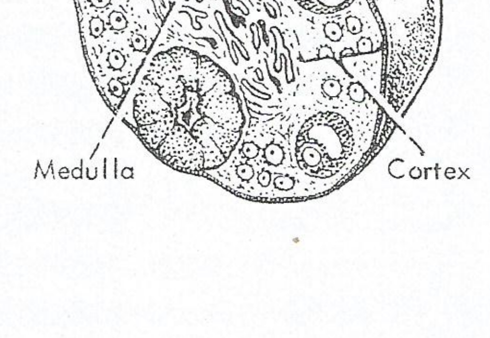
- From back of cervix to middle sacral piece
- Formed of 2 pairs (*surrounds the rectum*)
- THE ONLY TRUE lig.; ¤ → The only one that connects muscle (uterus) to Bone (sacrum).
  (others are condensed CT, smooth ms, elastic fibers)

DES: Diethyl stilbisterol: -synthetic Estrogen, was used (1940) for thr. abortion
leads to multiple anomalies. -It prevents normal vag. metaplasia from Columnar to st. sq. epithelium → Columnar epi. persists → vag. adenosis → vag. adeno Carcinoma within 30 y/s.

- Was stopped at 1970 d.t: → wrong drug. ↳ Teratogenic.







The only true intraperitoneal organ is the ovary.

- Fallopian tubes -

- Length →10 cm (4 inch)
- Extend from the cornu to open at the infundibulum
- Present in the free border of the broad ligament

▸ **Parts**

	Interstitial	Isthmus	Ampulla	Infundibulum
Length (cm)	1	2	5	2
Diameter (mm)	1	2	5	trumpet

- Largest fimbria is called fimbria ovarica → important for ovum pick-up
- The utero-tubal sphincter is found at the tubal ostia to:
  - Prevent retrograde menstruation into the pelvis
  - Delay the fertilized ovum for 3 days (till maturation)

▸ **Layers**

- **Peritoneal covering** → complete except the interstitial part¤ & a narrow strip opposite the attachment to broad ligament
- **Muscle** → inner circular & outer longitudinal
- **Endosalpinx** → thrown into folds. Cells are columnar partially ciliated, partially secretory ± *peg* cells (immature or reserve cells)

Racemose gl. → Milk tube for nutrition of fetus.

▸ **Blood supply** ⇔ uterine & ovarian vs (double supply ∴ tubal gangrene is rare)

- Ovary -

▸ **Position**

- Lies in the fossa ovarica (a depression in the lateral pelvic wall)
- The ureter & int. iliac artery are passing longitudinally behind it
- ***Connected*** to back of broad ligament by *mesovarium*¤
- ***Connected*** to uterus by *ovarian ligament*
- ***Connected*** to pelvic side wall by *infundibulopelvic ligament*

▸ **Size** *almond* shaped → 3 x 2 x 1 cm (5 gm)

▸ **Structure**

- *Hilum* → vessels, lymphatics, nerves enter & leave through it
- *Medulla* → vascular CT stroma............................small in size
- *Cortex* → follicles, corpus luteum & albicans......main compartment

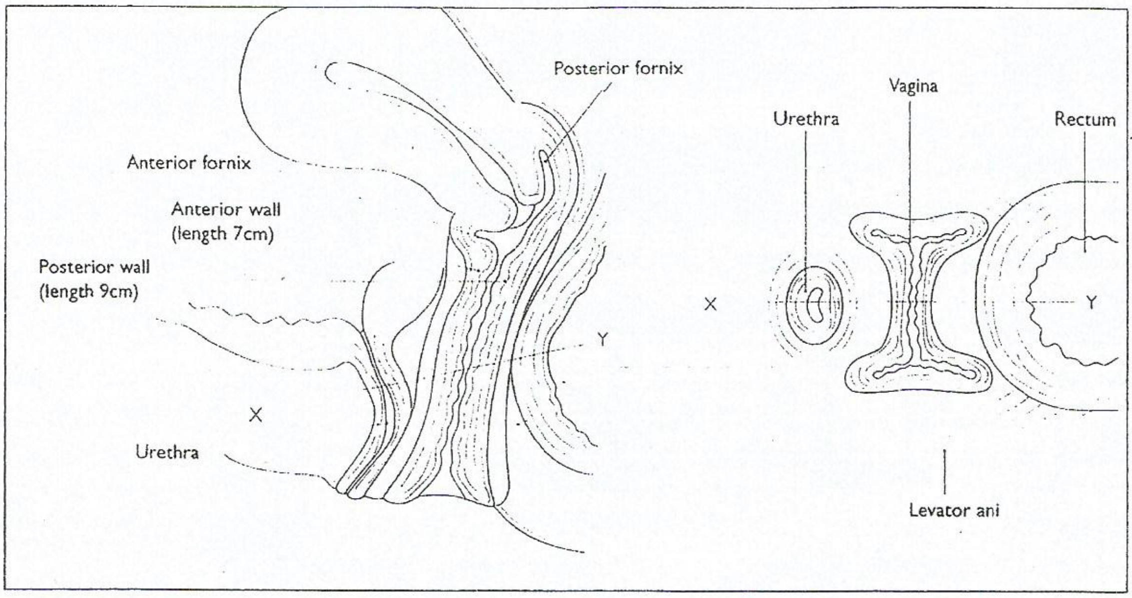
▸ **Covered by:-** *Tunica albuginea* → coelomic cuboidal epithelium ✓ → Thin layer.

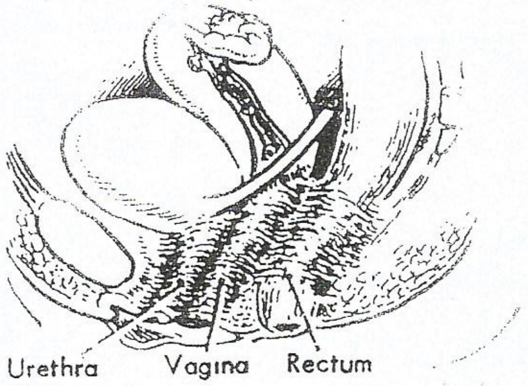
↘ Previously known as germinal epithelium ✗

↘ Ovary is *Not covered by peritoneum*¤ ***'to allow ovulation'***

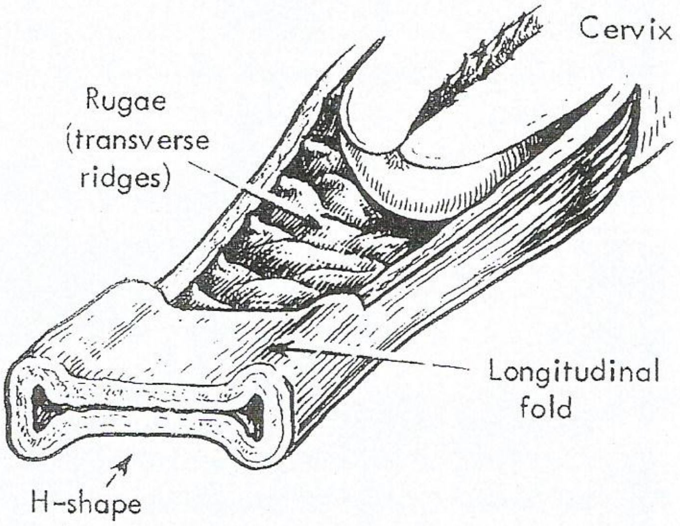
▸ **Blood supply** ⇔ ovarian artery

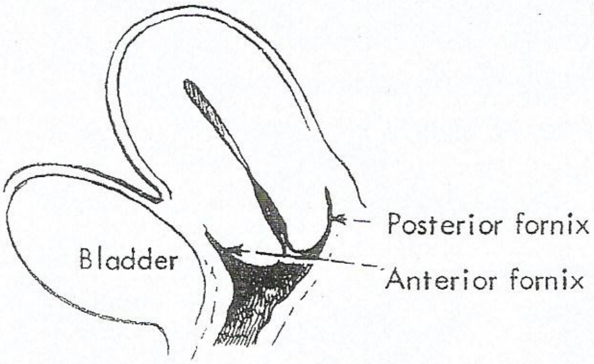
▸ **Lymph drainage** ⇔ paraortic LN¤

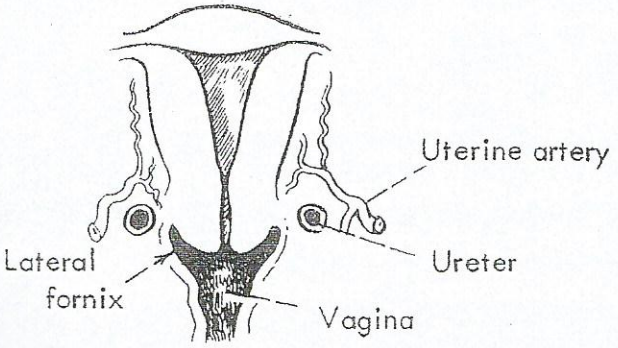


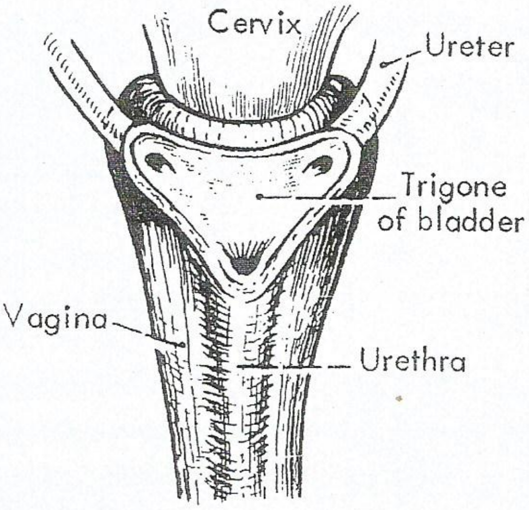


Lateral View. Note the close relationship to urethra, bladder and rectum.









- Vagina -

▸ **Structure**

- Elastic fibromuscular canal extending from vulva to uterus
- The orifice is partially closed by hymen in virgins
- Cervix projects into the upper part of *anterior wall* → 4 fornices ¤

  Anterior shallow..........Posterior deep.........2 lateral fornices

  ∴ the anterior wall is **8** cm while posterior wall is **10** cm ¤

▸ **Relations**

- Ant. ⇨ lower ⅓: (urethra)........upper ⅔: (bladder)
- Post.⇨ (lower ⅓: perineal body)...(mid ⅓: rectum)...(upper ⅓: D.pouch)
- Lat. ⇨ ureter.....levator ani & ischiorectal fossa....Bartholin gland

▸ **Wall**

- ***Two walls*** (anterior + posterior) opposed to each other (potential space)
  - transverse section......⇨.....H-shaped
  - longitudinal section....⇨.....Flask shaped
- ***Muscle*** → 2 layers (outer longitudinal, inner circular)
- ***Epithelium*** **(mucosa, vag. skin)**

  1] Stratified squamous epithelium non-keratinized

  2] Thrown into folds (rugae → allow distensibility)

  3] No glands ✓ ¤

  * Secretions come from ❶ cervix ❷ vag. transudation ❸ Bartholin

  * Except after maternal exposure to DES ⇨ vaginal adenosis

  4] Glycogen rich, E dependent → ↑ thickness +↑ glycogen + ↑acidity (through Doderlein bacilli = pH 3.5–4.5) → protective effect

.After puberty & in newborn (maternal E) → thick + ↑glycogen + acidic
.Prepubertal & postmenopausal → thin + no glycogen + alkaline

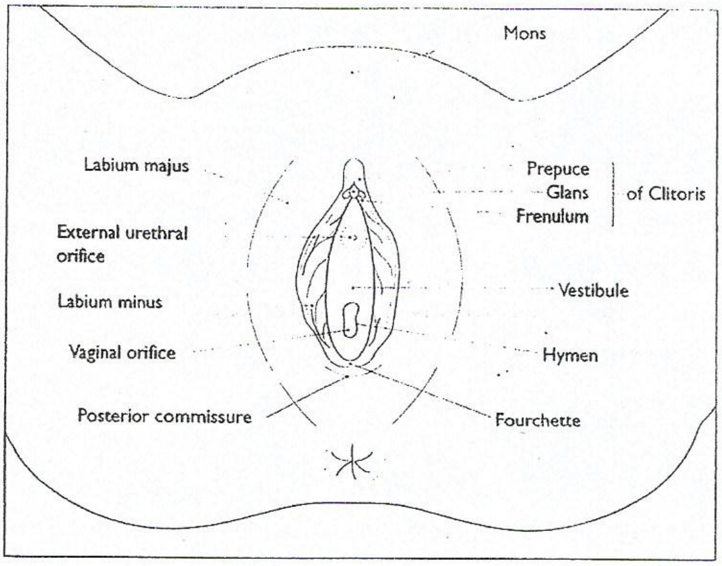
▸ **Blood supply......very rich......** ⊷

- **Uterine** →. circular artery of cervix → ant. & post. azygous arteries
  . descending cervical a. (cervicovaginal a.)
- **Internal iliac artery** → middle rectal artery, **vaginal artery**
- **Internal pudendal** → inferior rectal artery

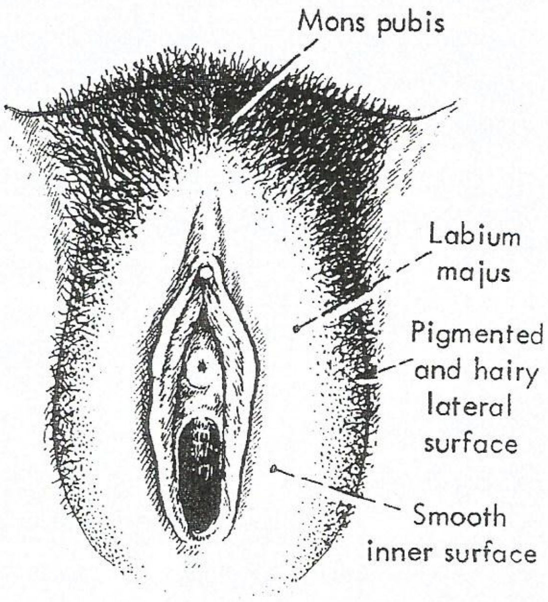
▸ **Nerve supply** ⇨ upper part (insensitive)............lower ¼ → (pudendal n)

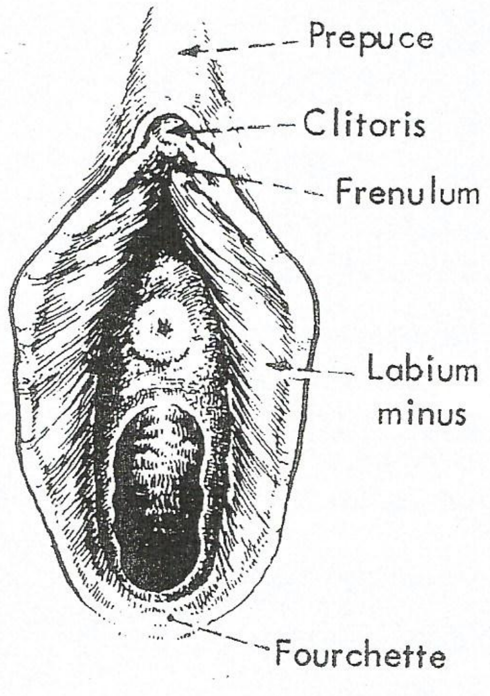
▸ **Lymphatics** ⇨ upper part with cx......................lower ¼ with vulva

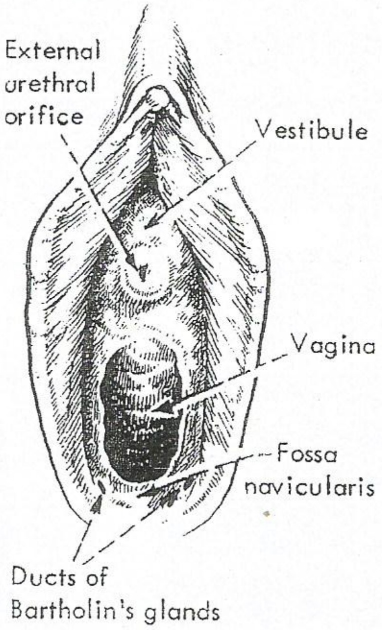
▸ **Vaginal support** ⇨ attachment to cervix......cx ligaments.....levator ani



The vulva of a virgin.







The External Genitalia (Vulva - Pudendum) Φ

1-Mons Pubis (mons veneris)

- Pad of fat covering symphysis pubis → act as *cushion* during intercourse
- Covered by inverted ∇ hair, while in male → apex may reach umbilicus

2-Labia majora (labium majus)

- Two longitudinal *elliptical* skin folds, extending:
  - Above → from the mons pubis
  - Down → join together posteriorly at the *posterior commissure*
- Formed of:
  - Skin (keratin + hair follicles + subcutaneous fat)¤
  - Sweat (apocrine) glands → secretions with ccc odour
- Occasionally they contain *canal of Nuck*¤ (a fold of peritoneum)

3- Labia minora (nymphae)

- Two skin folds enclosed within the labia majora, each one will
  - Split anteriorly to enclose the clitoris:-
    - . The upper flap will form → the *Prepuce* anteriorly
    - . The lower flap will form → the *Frenulum* posteriorly
  - Join together posteriorly to form → the *fourchette*
    - . The depression between the fourchette & hymen is¤ present only in virgins & called *fossa navicularis*
- Formed of
  - Thin redundant skin (no-keratin + no hair follicles + no fat)¤
  - Pink colored → vascular connective tissue

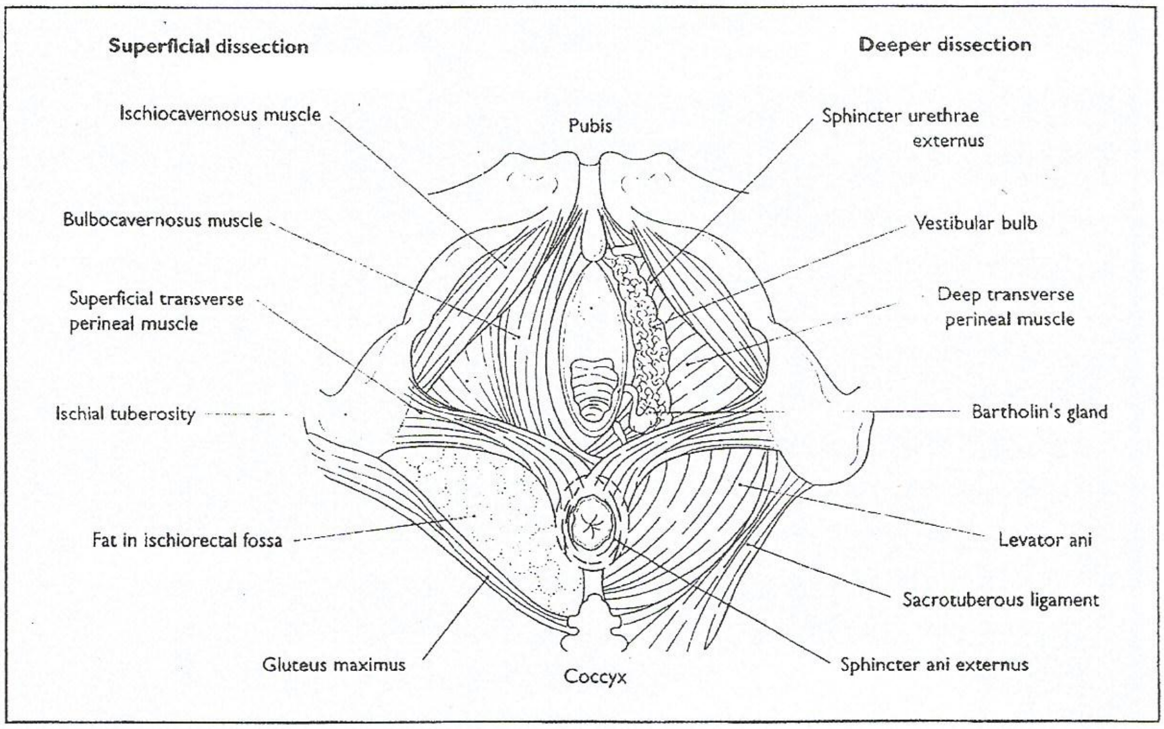
4- Clitoris

- **Length** ⇨ 2–3 cm long¤ ....2–3 cm above urethra¤
- **Def.** ⇨ v. *sensitive* (⇧ nerve supply) *erectile* (2 corpora cavernosa) tissue
- **Parts** ⇨ *Glans* (between prepuce & frenulum)......*body*.....*2 crura*

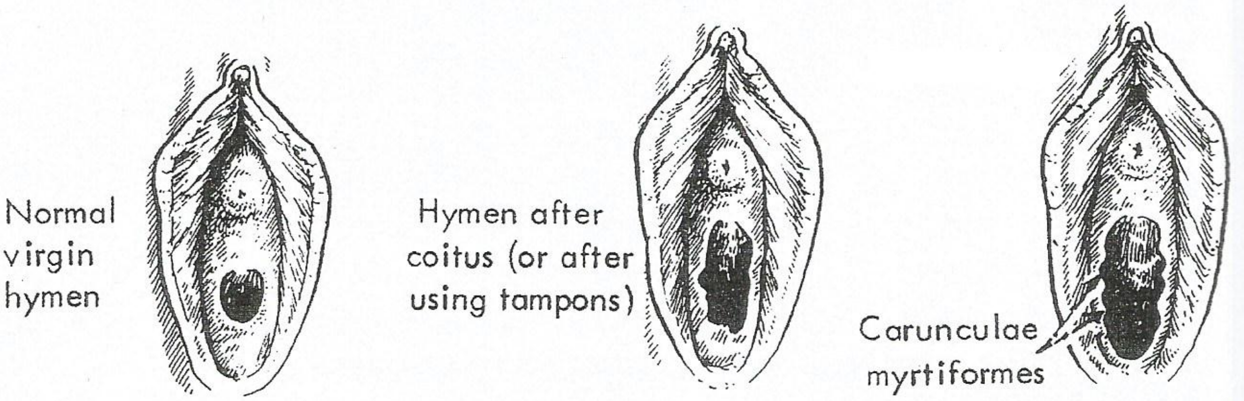
5- Vestibule

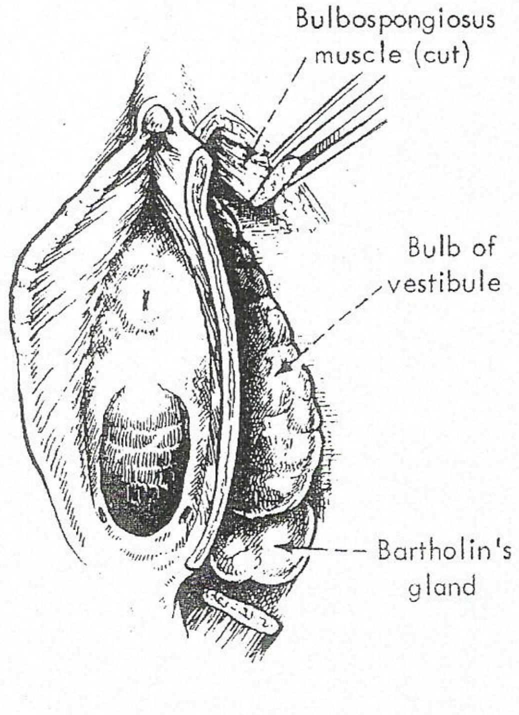
- The area¤ within the two labia minora) It receives the openings of:-
  - External urethral meatus
  - Vaginal introitus (orifice)
  - 2 Bartholin ducts

structures w disappear after 1st Inter course: (Present only in virgin).
1-Hymen 2-fossa navicularis 3-fourchette



Dissection of the perineum to show the superficial muscles, the position of Bartholin's gland and the vestibular bulb.





6- Vestibular bulbs

- Two small collections of vascular spongy C.T.
- They lie on either sides of vaginal opening → act as a cushion
- They are continuous above with the clitoris
- They lie deep to *bulbo-spongiosus* muscle

7- External urethral meatus

- The female urethra is 4 cm long ¤
- Urethra is lined by transitional epith.....the ext. meatus → st.sq.epith ¤
- Two paraurethral glands (*Skene's gland*) open in its floor 1 cm before the external urethral meatus

8- Hymen

- Thin membrane partially separating **vaginal orifice** from **vestibule**
  - Formed of ⇨ CT lined on both sides by stratified sq. epithelium
  - Types ¤ ⇨ cresentic, septate, cribriform, ***annular*** ✓, ***imperforate*** ✗
- **After defloration** (1st coitus) → *slight spotting* (relatively vascular)
- **After labor** → remnants are called: *caraunculae myrtiformis*

9- Bartholin (greater vestibular) Glands

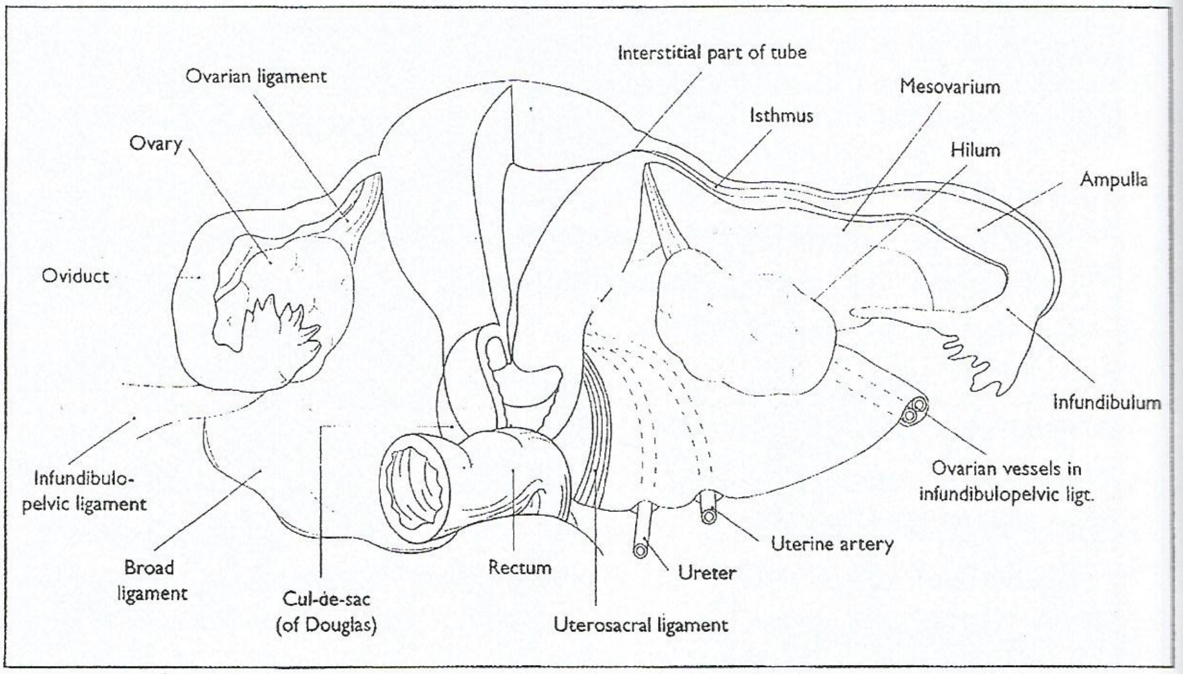
- ***Site***: . One on either side of the vagina
  . Embedded in the posterior ⅓ of the vestibular bulb ¤
- ***Structure***
  - Size of a pea (normally can't be felt except if *infected*: *abscess*)
  - Compound racemose glands, Its duct is 2–3 cm long → opens on either side of the vaginal introitus (5, 7 o`clock)
- **Function**: alkaline vaginal secretion for lubrication during intercourse

---

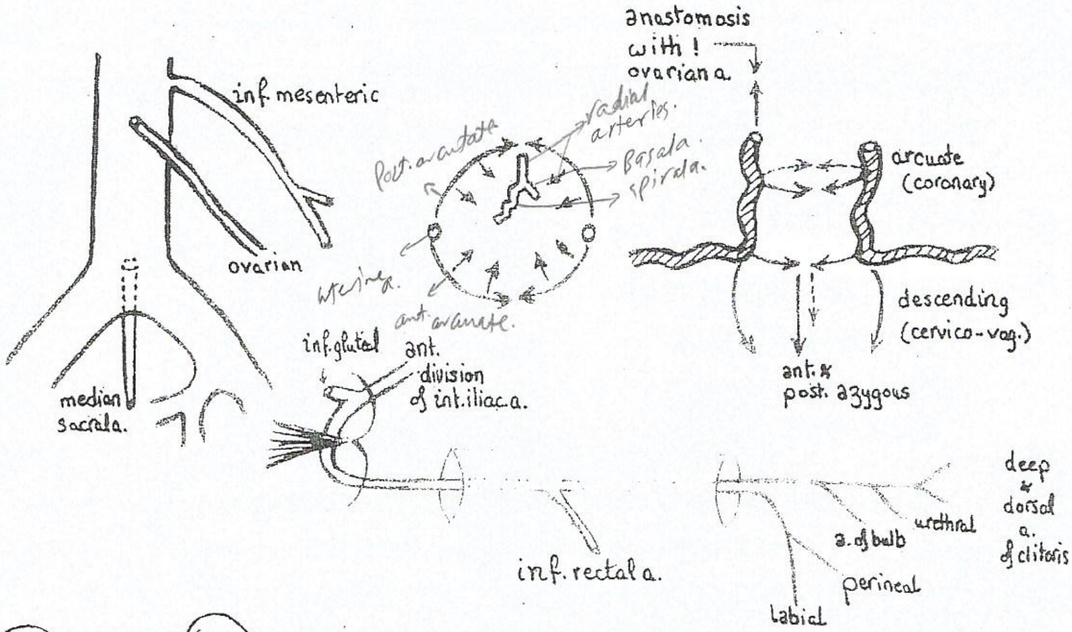
Blood supply ¤ ⇨ - **Internal pudendal artery** (*mainly* ¤)
- Femoral a. (superficial & deep external pudendal)

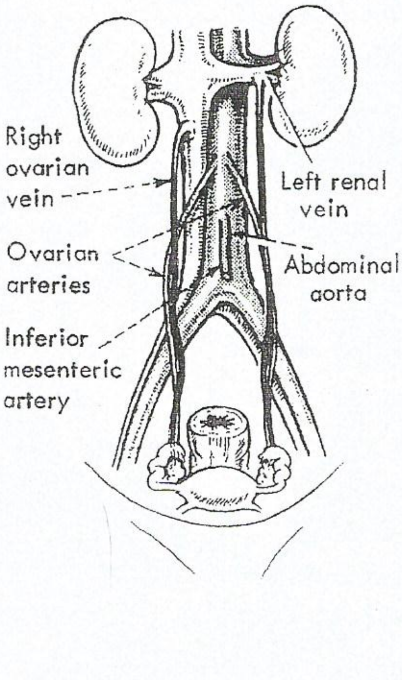
Nerve supply ¤ ⇨ - **Pudendal n.** (motor & sensory) Φ
- Sensory supply *also* from:
  1. Perineal br. of lat. & post. cutaneous n. of thigh
  2. Ilioinguinal, iliohypogastric
  3. Genital branch of genitofemoral n.

Lymphatics ⇨ as in cancer vulva: **groin LN** (inguinal & femoral)
⇨ each side drains to both corresponding & opposite LN, then
⇨ external iliac → common iliac → paraortic LN

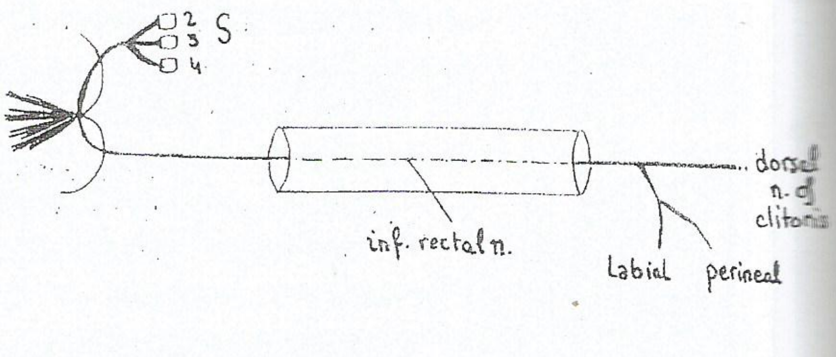


The female pelvic organs viewed from behind. On the left the oviduct and ovary are in the position found in vivo; on the right dissection has been made.





- Pudendal nerve -



Tortous arteries in the body:
1- Uterine a.
2- Facial a.
3- Lingual a.
4- Splenic a.

- Blood supply of Pelvis -

▸ Internal iliac artery ¤ ΦΦ

Anterior division	Posterior division I/L S
1- Visceral	1- Ilio-lumbar
* Uterine	
* Superior vesical (obliterated umbilical) → lat. umbilical lig. (continuation)	2- Lateral sacral
* Inferior vesical (vaginal) → maybe continuation of vesical a. / 2 branches from one stem or as separate br. from Ant. division	
* Middle rectal (hemorroidal)	3- Superior gluteal
2- Muscular branch (obturator)	
3- Terminal branches (inf.gluteal, int.pudendal)	

NB - Superior rectal a. ⇔ continuation of inferior mesenteric artery ¤
- Inferior rectal a. ⇔ a branch of internal pudendal artery

▸ Uterine artery

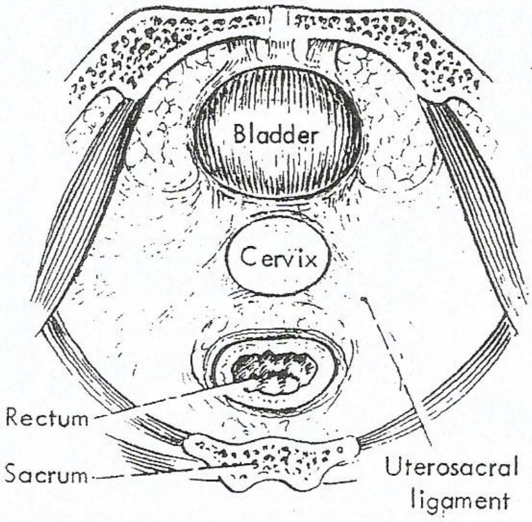
- The main vessel, a branch from the anterior division of IIA
- They are tortuous (to allow uterine expansion during pregnancy)
- It runs *medially* to cross **above** ¤ the lower end of the ureter
  2 cm ← lateral to the supravaginal part of the cervix
- Then it turns *upwards* at the lateral border of the uterus within the leaflet of the broad ligament.
- Branches:
  . To the ureter
  . Circular branch → to the cervix (anastomose ant. to form ant. azygos a.; post. to form post. azygos a.)
  . Descending branch → to the vagina (cervico-vaginal)
  . Ascending branch → gives arcuate (coronary) arteries
  ∴ the midline of the uterus is the least vascular

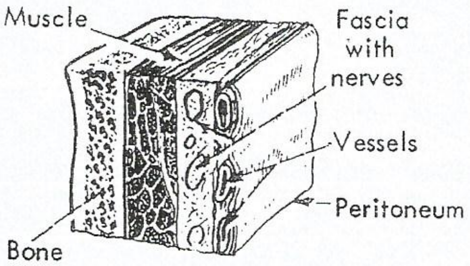
Radial arteries arise from the anterior & posterior arcuate arteries to perforate the endometrium. They will finally divide to 1- *Basal artery*....supplies basal parts only 2- *Spiral artery*...supplies the more superficial parts

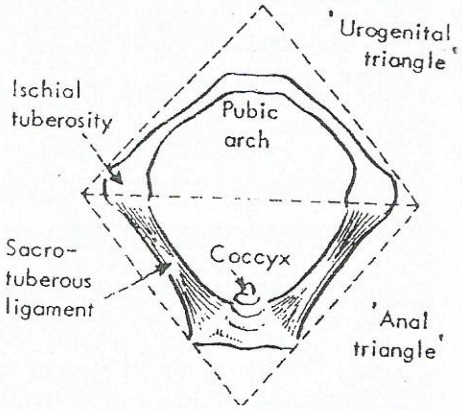
. Finally, it anastomoses with branches of ovarian a. at the cornu ¤

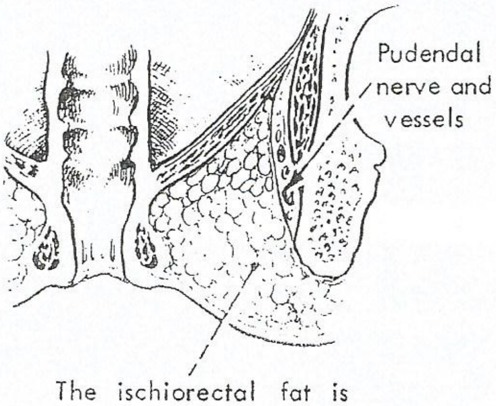
▸ Ovarian artery

- Arises from aorta at L_2 (just below the renal artery) ¤
- At the pelvic brim, it crosses the external iliac vessels & enters the pelvis in the *infundibulo-pelvic ligament* to reach the mesovarium and enter the ovary through the hilum
- Left ovarian vein → drains into the left renal vein ¤
- Right ovarian vein → drains into the inferior vena cava ¤



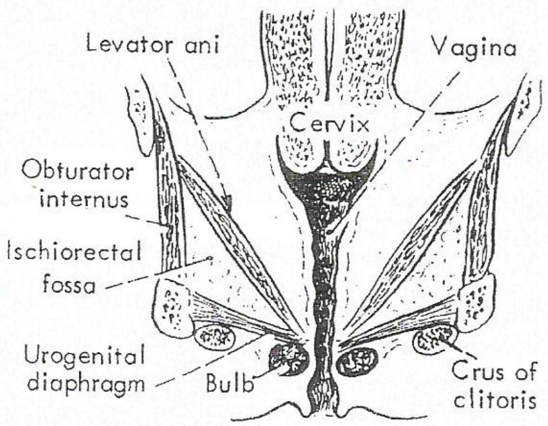




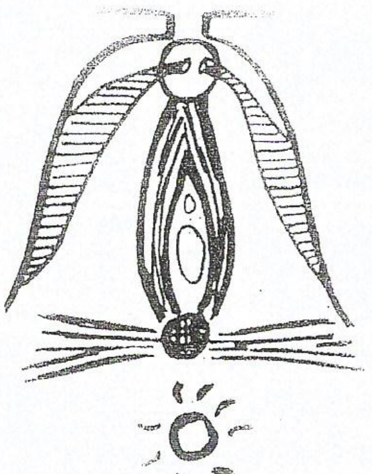


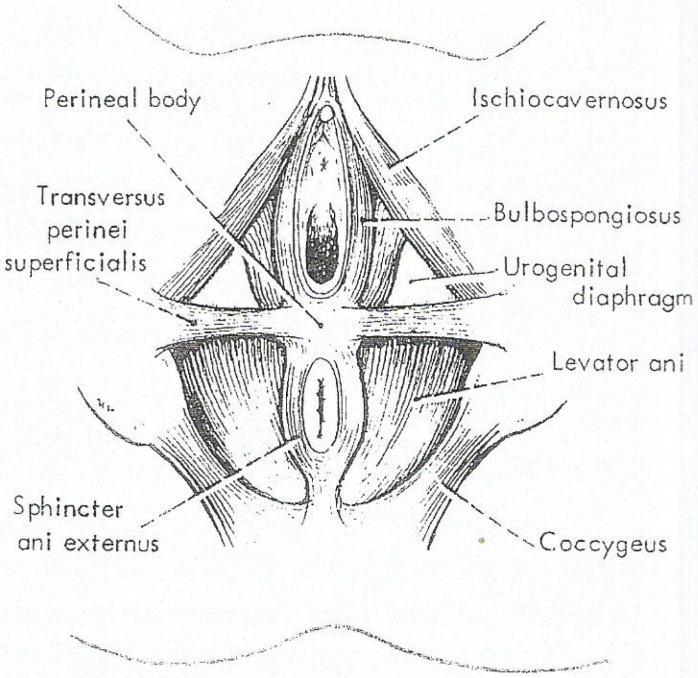
The ischiorectal fat is traversed by the pudendal vessels and nerves and some small perineal branches of sacral nerves.

This pad of fat supports the anal canal and pelvic diaphragm.



Coronal section shows the relationship of vagina and pelvic floor.





Covers the whole uterus
- Cx → Ant wall → No periton., Post wall → covered.
- Vag → " " --, Post wall (upper part) → covered.

- Pelvic Floor -

[1] Pelvic peritoneum

- It extends from over the ***bladder*** to the Uterovesical pouch then over the ***uterus*** then to the **posterior** surface ¤ of *cx* & ***vagina*** (Douglas pouch)¤ then to the anterior surface of the ***rectum*** (lower ⅓ of rectum not covered)¤
- Laterally → the two peritoneal folds form the ***broad ligament***

[2] The pelvic fascia

- It is divided into 2 parts
  - **Parietal fascia** ➡ covers the muscles of pelvis
  - **Visceral fascia** ➡ endopelvic fascia, pelvic cellular CT
- This fascia forms certain strong condensations
  - Cervical ligaments (3)
  - At the base of broad ligament ➡ parametrium
  - Around the vagina ➡ paracolpos
  - Between the vagina & rectum ➡ rectovaginal fascia

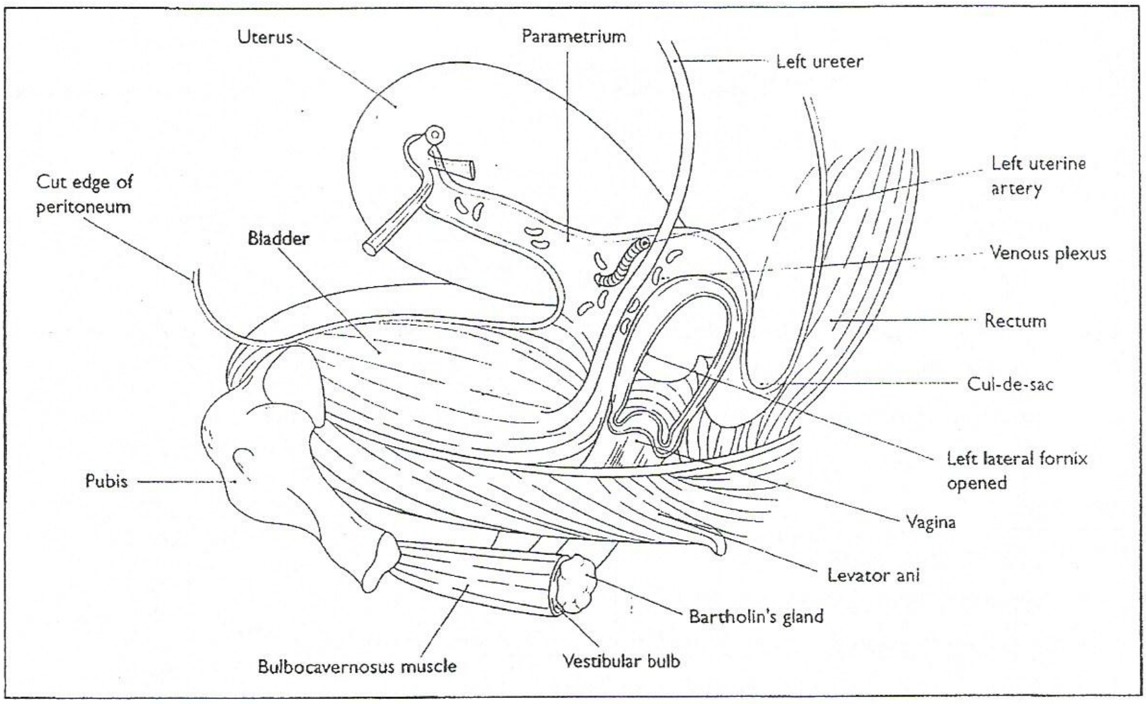
[3] Pelvic diaphragm

- A fibromuscular sheet which supports pelvic contents
- It extends as a diamond shape from the lower border of SP to the 2 ischial tuberosities till the tip of coccyx
- It is composed of (2 levator ani & 2 coccygeal muscles) & their supporting fascia (superior & inferior pelvic fascia)
- It is divided into 2 triangles
  - The urogenital triangle (diaphragm).....anterior
  - The anal triangle...........................posterior

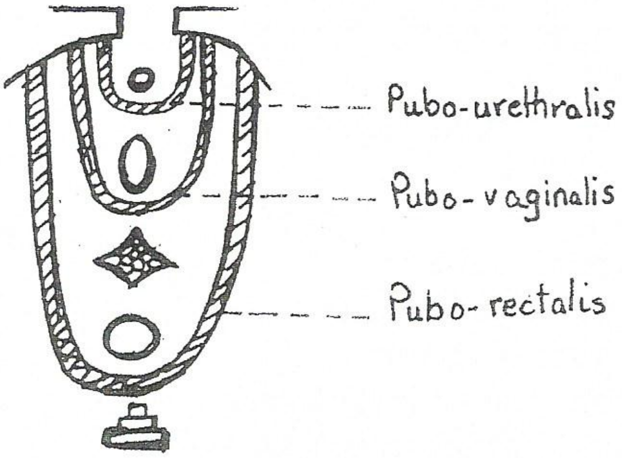
[4] Perineum... 2 - 5 cm

- The area extending between skin (below) & the pelvic diaphragm (above)
- Divided into 2 pouches (superficial & deep) separated by a perineal memb

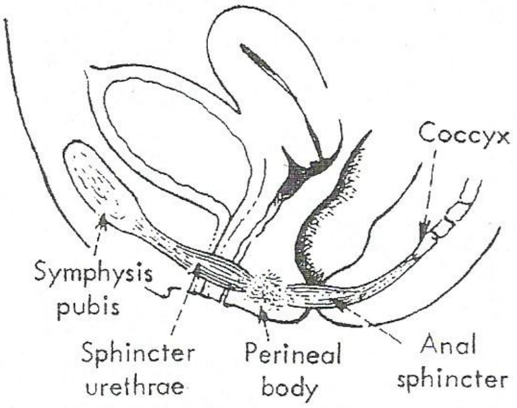
- **Perineal body**
  - Fibromuscular pyramidal condensation
  - Lies between vagina & anal canal
  - Formed by decussation of 8 muscles
- **Ischiorectal fossa**
  - Wedge shaped space on either side of anal canal filled by fat
  - Boundaries
    - . Superior & medially → levator ani
    - . Lat.→ obturator ms & fascia (splits to form *pudendal*: Alcock's canal)
    - . Inferiorly → skin



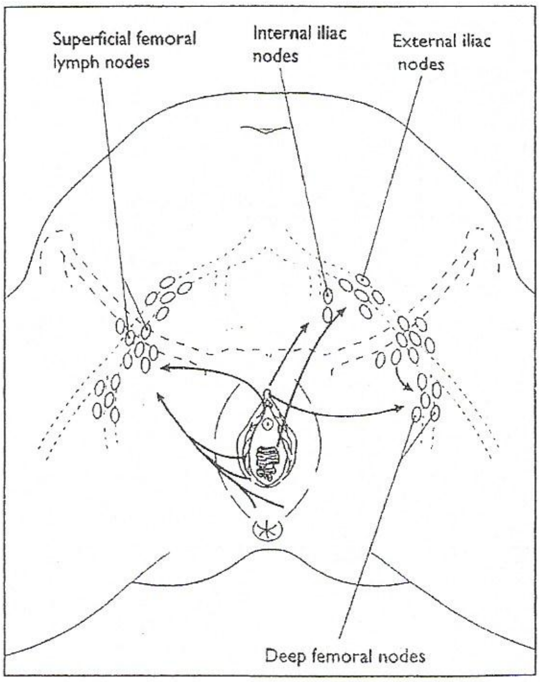
Uterus
Parametrium
Left ureter
Left uterine artery
Cut edge of peritoneum
Bladder
Venous plexus
Rectum
Cul-de-sac
Left lateral fornix opened
Pubis
Vagina
Levator ani
Bartholin's gland
Bulbocavernosus muscle
Vestibular bulb



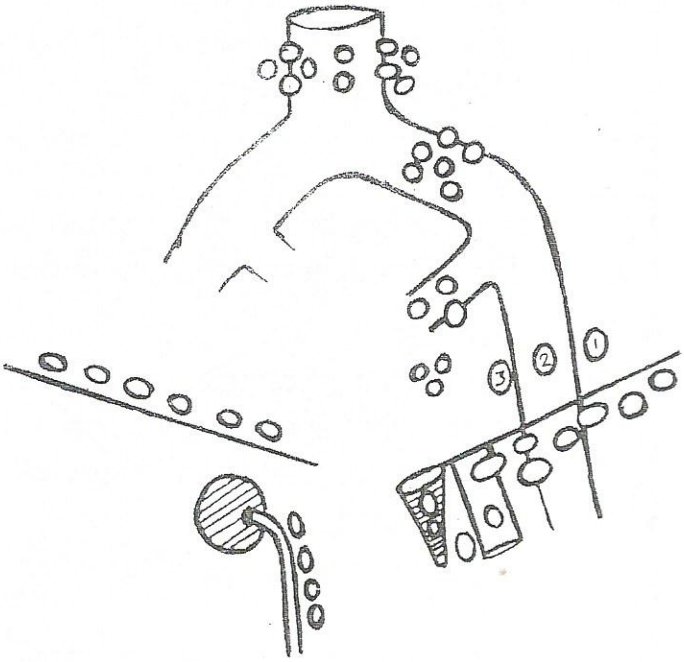
Pubo-urethralis
Pubo-vaginalis
Pubo-rectalis



Coccyx
Symphysis pubis
Sphincter urethrae
Perineal body
Anal sphincter



Superficial femoral lymph nodes
Internal iliac nodes
External iliac nodes
Deep femoral nodes



1
2
3

- Levator ani -

➡ **Pubococcygeus**

- Origin: From back of S. pubis & anterior part of white line (a thickening in the obturator fascia)
- Insertion:
  - Side walls of urethra → *Pubourethralis*
  - Side walls of vagina → *Pubovaginalis* (fibers of Lushka)
  - Side walls of rectum → *Puborectalis*
  - Tip of coccyx & anococcygeal raphe → *pubococcygeus* proper

➡ **Iliococcygeus**

- From white line to perineal body, anococcygeal raphe & coccyx

➡ **Ischiococcygeus**

- From ischial spine to coccyx & sacrum

Nerve supply

* Pudendal n. S_{234} → perineal surface (covered by inf. pelvic fascia)
* Branches of S_{34} roots → pelvic surface (covered by sup. pelvic fascia)

Function

- Support of viscera
- Maintain intrabdominal pressure
- Sphincter to urethra, vagina & rectum
- Important role in labor (rotation)

ΦΦ - Lymphatic drainage ¤¤ - ☠☠

➊ The femoral LN (longitudinal)

- Superficial.....along the saphenous vein
- Deep.....along the femoral vein (esp. LN of *Cloquet*: in femoral canal)

➋ The inguinal LN (transverse)

- Superficial.....below & parallel to the inguinal ligament
- Deep.....present in the inguinal canal

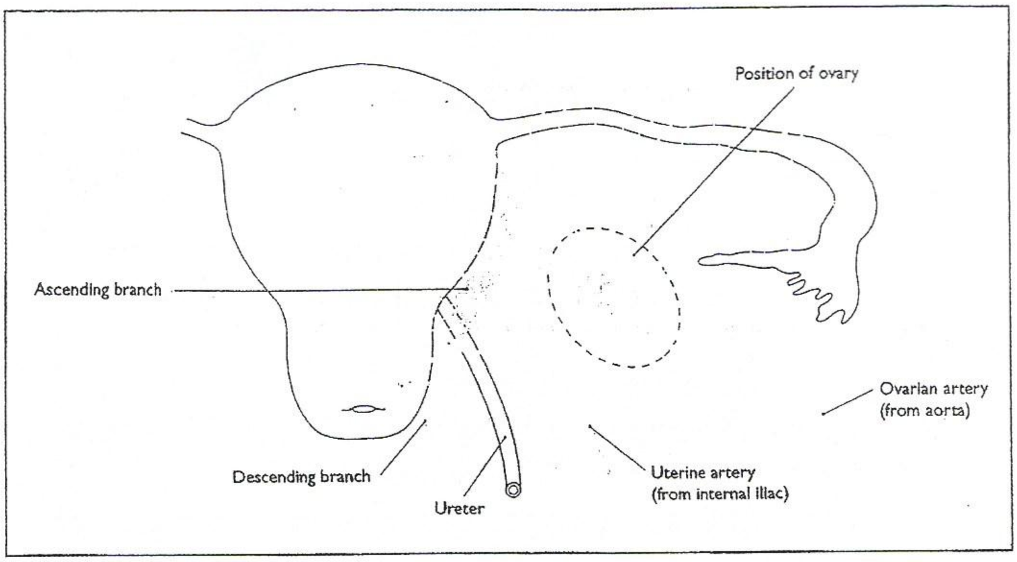
➌ The cervical LN

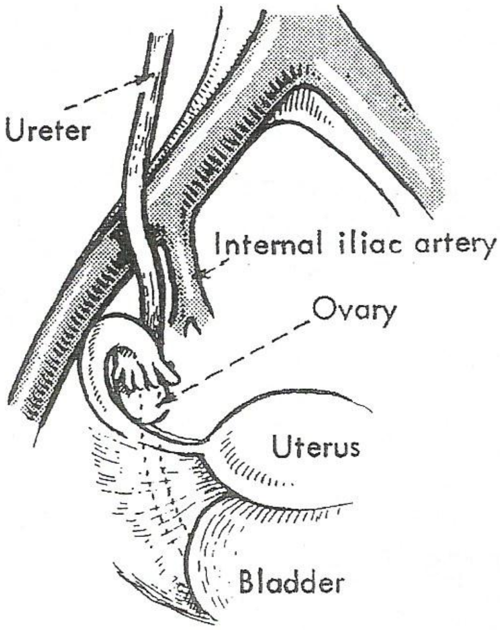
- Paracervical + Parametrial + Ureteric + Presacral

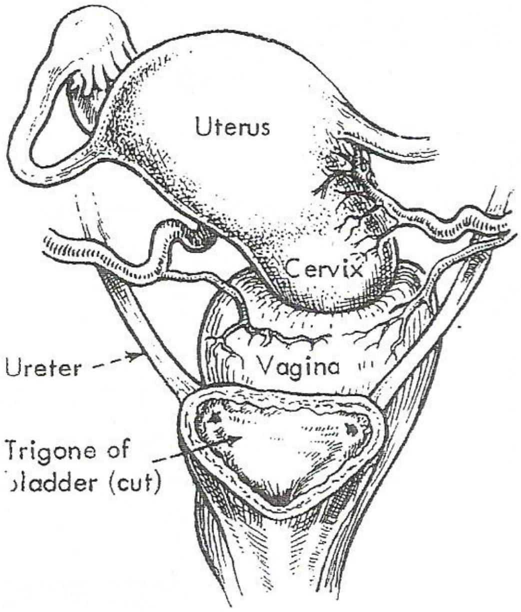
➍ The iliac LN

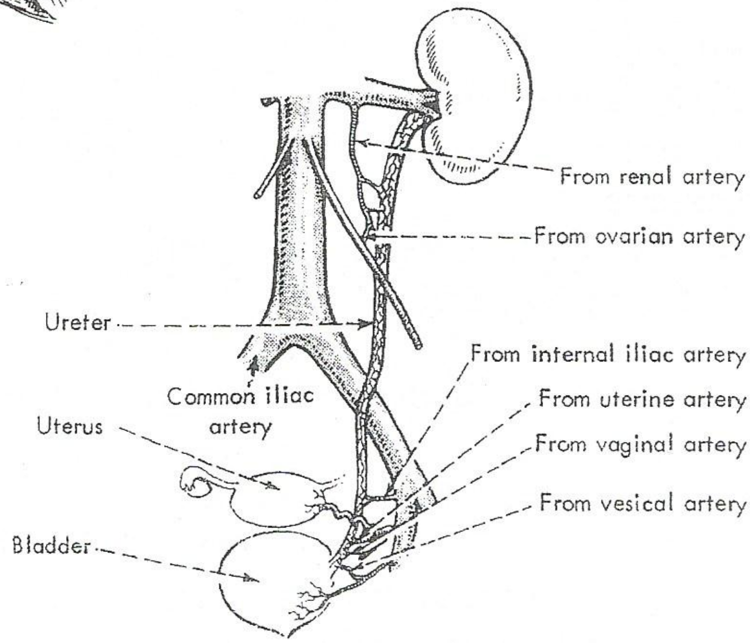
- Internal iliac...............along internal iliac vessels
- External iliac.............. 2- ANTERIOR, 3- MEDIAL, 1- LATERAL groups
- Obturator (interiliac)......near the obturator foramen
- Common iliac...............along the common iliac vessels

➎ The paraortic LN


Position of ovary
Ascending branch
Ovarian artery
(from aorta)
Descending branch
Uterine artery
(from internal iliac)
Ureter


Ureter
Internal iliac artery
Ovary
Uterus
Bladder


Uterus
Cervix
Ureter
Vagina
Trigone of
bladder (cut)


From renal artery
From ovarian artery
Ureter
Common iliac
artery
From internal iliac artery
From uterine artery
From vaginal artery
From vesical artery
Uterus
Bladder

- Pelvic Ureter -

▶ **Course (10–15cm)**

* The ureter enters the pelvis by *crossing the bifurcation* of the common iliac artery.
* It then passes downwards *infront* the internal iliac vessels to become *medial* to them & *behind* the infundibulopelvic ligament & ovary
* Just above the level of the ischial spine, it curves medially & forwards to pass through the *ureteric canal* (in the Mackenrodt ligament) till it reaches the bladder trigone
* It is *crossed by the uterine artery* ¤ at the base of the broad ligament. Here the ureter is *2 cm lateral to cx* & *2 cm above vaginal vault*

▶ ∴ **It may be injured in many gynecological procedures**

As it passes almost near to all genital structures

This is due to close embryological origin e.g. during:- Φ

- Hysterectomy (abdominal or vaginal)
- Pelvic lymphadenectomy
- Bilateral internal iliac artery ligation
- Adenexectomy (removal of ovarian swellings)

Injury is increased in

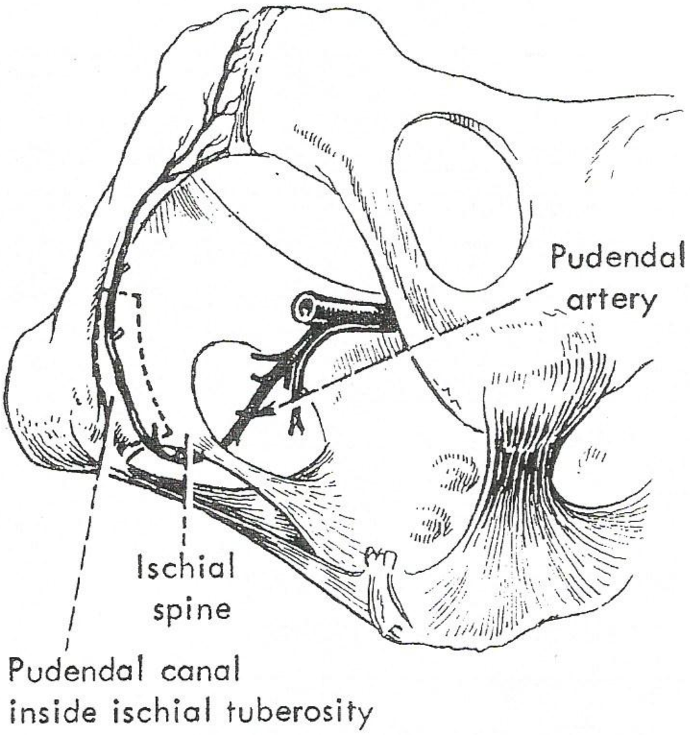
- Distorted anatomy
  - Congenital → malformations of the genital or urinary tract
  - Acquired → cervical fibroid, broad lig. swelling, extensive adhesions ✓
- Rapid blind clamping ✓ to stop massive bleeding

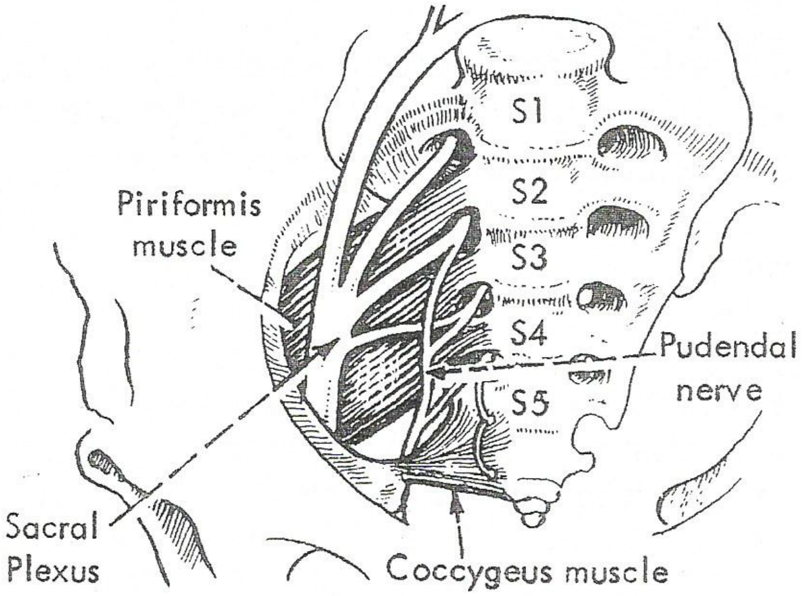
▶ **To avoid injury, we must do**

- Pre-operative ⟹ *IVP*
- Intra-operative
  - Proper identification of its *anatomical* course
  - Clamping must *only* be done under vision
  - Clamping must be *near* to the uterus

*** Injury may be**
- Direct → cutting, crushing, suturing
- Indirect → devascularization in radical hysterectomy / post-radiation

*** Leads to**
- Hydroureter → hydronephrosis → renal atrophy
- Fistula formation


Pudendal
artery
Ischial
spine
Pudendal canal
inside ischial tuberosity


S1
S2
S3
S4
S5
Piriformis
muscle
Pudendal
nerve
Sacral
Plexus
Coccygeus muscle

- Female genital mutilation -

Magnitude of the problem

- It means all procedures that involve partial / total removal of external genitalia for *cultural non-therapeutic reasons*
- It is still practiced in Egypt, Sudan (tradition? African? religious?)
- It is totally condemned by WHO; practiced only if
  - * Cosmetic (chafing: roughness)
  - * Simple hypertrophy of labia minora (dyspareunia)
  - * Nymphomania

WHO classification

- **Type I** ⇒ excision of part (prepuce) or the whole clitoris
- **Type II** ⇒ as above + labia minora
- **Type III** ⇒ excision of all external genitalia + narrowing of introitus (Sudanese circumcision, infibulation)
- **Type IV** ⇒ unclassified e.g. piercing, tattooing

Complications ΦΦ

immediate	later on
. Severe pain . Hemorrhage, infection . Injury to urethra	. Psychological, sexual troubles . Recurrent UTI . Retention dermoid cyst . Obstructed labor d.t. fibrosis

- Nerve supply -

☆ **Uterus, cervix, upper vagina ⇒ autonomic:**

1- Sympathetic $T_7 \rightarrow L_2$

Postaganglionic fibers pass in the **(superior hypogastric plexus)** over the promontory of sacrum & divides into ❶ right & left presacral nerves (on both sides of the rectum)

2- Parasympathetic $S_{2,3,4}$

Preganglionic fibers (❷ Pelvic / Splanchnic) pass along with the pudendal nerves → relay at ganglia in or near wall of viscera

☆ NB

- *The pelvic plexus* **(inferior hypogastric plexus)** = ❶ + ❷
- The cervix is *only* sensitive to dilatation
- The body is *only* sensitive to distension
- Vulva, perineum, lower ¼ vagina ⇒ all somatic

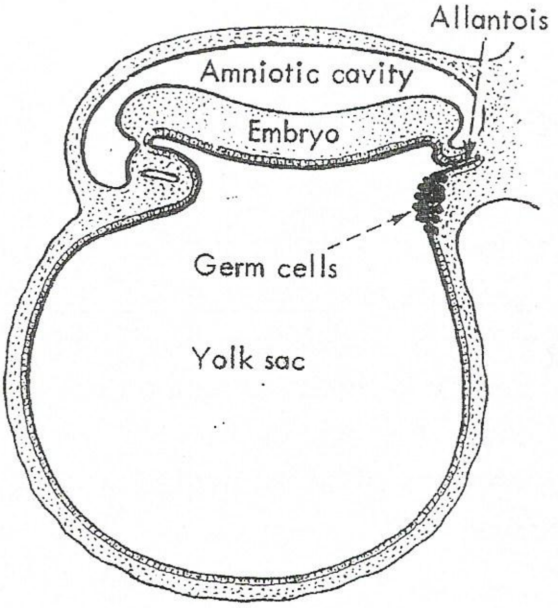
-) Theca cells: Converts Cholesterol → P. → Androgen.
- Granulosa cells: Convert Androgen → E By Aromatase enz

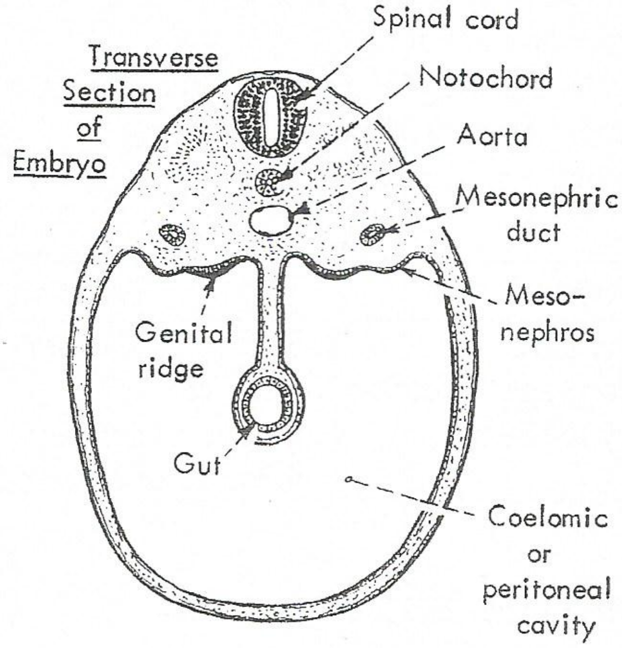
Hypo- ↓ GnRH
Pit. ↓ Gonado Trophins FSH, LH
ovaries ↓ E+P.

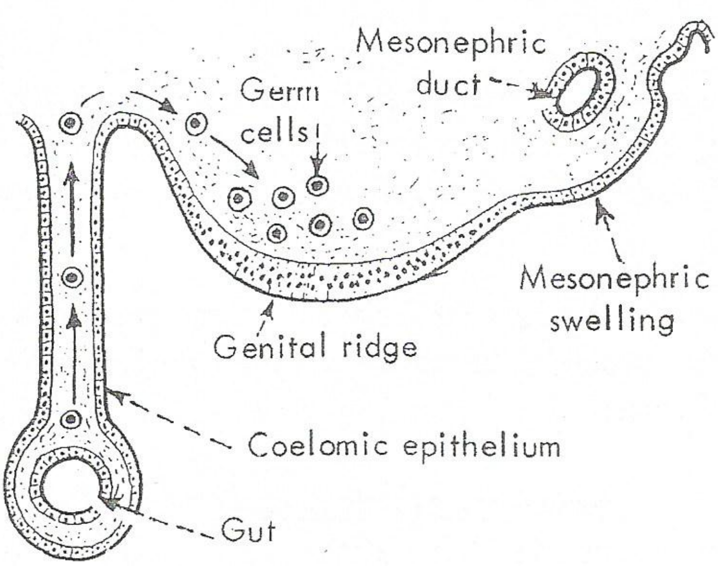
-ve Feedback

Biological Amplification

نظرية كرة التلج
كلما تنزل للتحت تكبر







* Presence of 2 Polar bodies is a sure sign for fertilization.

Embryology

❶ Development of the ovary

♣ Intra-uterine

- The **primitive germ cells** appear in the wall of yolk sac (near the hindgut) at the 3rd week. These cells **migrate** along dorsal mesentery to reach the **genital ridge** (which is the medial thickened part of the urogenital ridge)

- Germ cells will markedly ↑ in number by mitosis to reach a maximum of 6-7 million at the 20th week. Then mitosis stops and the oogonia will start the 1st reduction division (meiosis) in which they will be **arrested in prophase**

- An out-growth from the surface epithelium into the substance of the ovary will form the **sex cords**, while some cells from the mesenchyme will form the **sex stroma**
  - *The sex cords envelop the oocyte to form the granulosa cells*
  - *The sex stroma will form the theca cells (as an outer layer)*

♣ At birth

A large number of 1ry follicles will be lost in intrauterine life by a process of apoptosis (programmed cell death). Thus, follicles are reduced to 1 million **at birth** → then atresia occurs following birth throughout life and the number is further ↓ to 400.000 at **puberty** ¤

♣ After puberty

A certain number of primordial follicles (400-1000) in each cycle will resume meiosis. Only 1 will become fully mature (the dominant follicle) ➠ 1ry oocyte + 1st polar body, while the remainder will undergo atresia. Upon fertilization, the 2nd meiotic division (mitotic like) will occur ➠ 2ry oocyte + a 2nd polar body

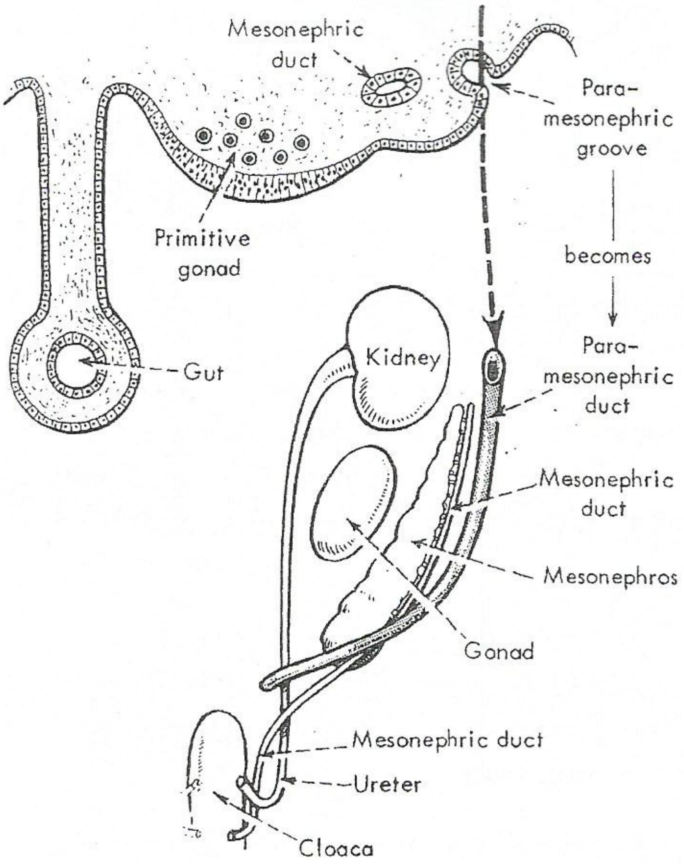
♣ Formation of ligaments ¤

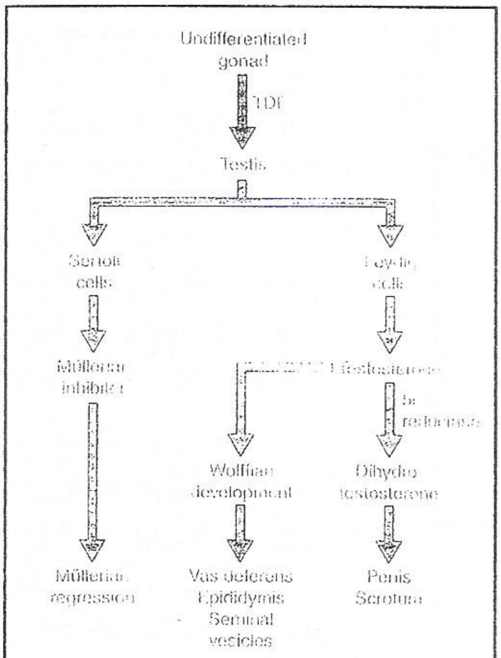
The lower part of the genital ridge becomes "gubernaculum", which gains attachment to the cornu of the uterus:

- The upper part of the genital ridge ⇨ **Infundibulopelvic lig.**
- Part between the ovary and the uterus ⇨ **Ovarian ligament**
- Part between the uterus and labia majora ⇨ **Round ligament**

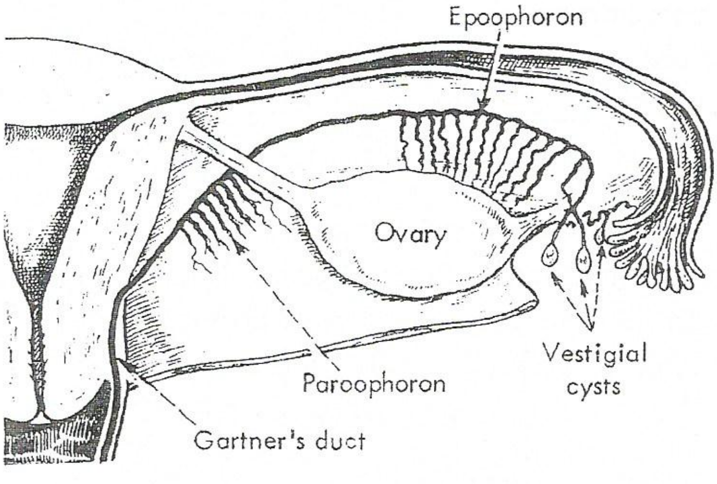
♣ Migration (descent ⇩) of ovaries ¤

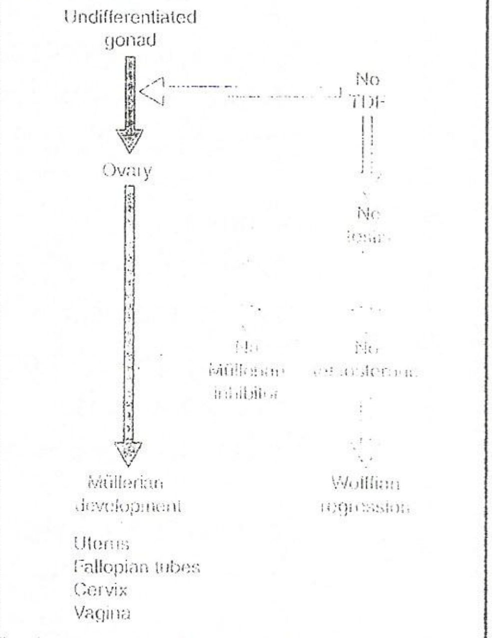
Descent of the *ovary* into pelvis is d.t. unequal body growth (trunk > rest of the body) & *not hormone dependent* (unlike the testis)



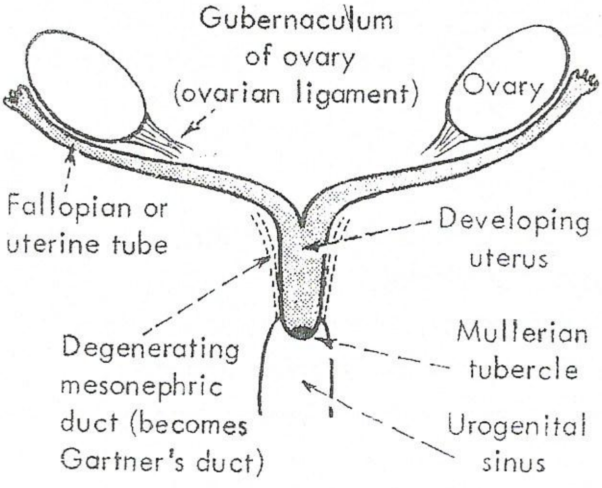


Male differentiation (TDF, testicular determining factor)





Female differentiation (TDF testicular determining factor)



❷ Development of the ductal system

In Males

- The *Wolffian duct* (mesonephric) *develops* under effect of
  SRY = Sex determining Region of Y chromosome)
  ↳ testosterone production from **Leydig** cells

- The *Mullerian duct* (para-mesonephric) *regress* under effect of
  MIF ¤ (Mull. inhibitory factor) = AMH (anti-Mull. hormone)
  ↳ produced by **Sertoli** cells in testis

- Vestigial remnants ¤ may be found between the 2 layers of broad lig & may lead to formation of large (paraovarian / br.ligamentary) cysts ¤
  1. KOBLET TUBULES ⟹ at outer part of broad ligament
  2. HYDATID OF MORGAGNI ⟹ near tubal fimbria
  3. EPOOPHRON ⟹ between ovary & tube
  4. PAROOPHRON ⟹ between ovary & uterus
  5. GARTNER DUCT ⟹ runs medially below the tube then → lateral to uterus, cx, vagina → ends at the clitoris (forms Gartner cysts)

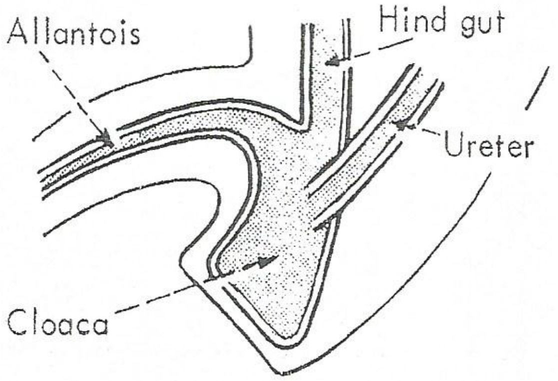
In Females

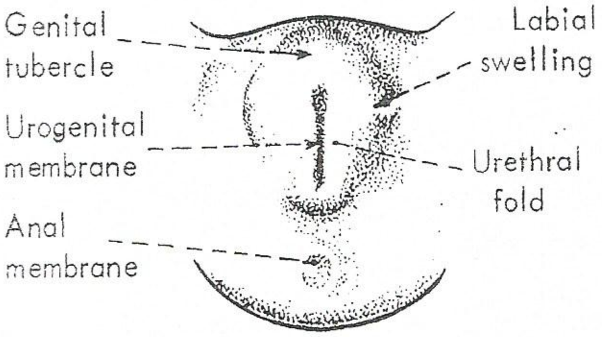
- **Indifferent stage:**
  The *Mullerian duct* develops in the lateral part of the urogenital ridge as a longitudinal invagination of the coelomic epithelium

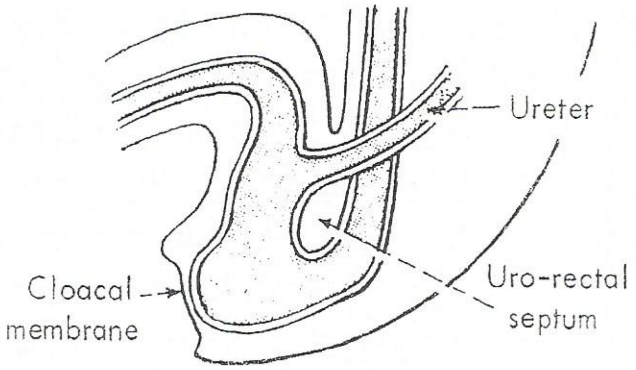
- **Control**
  - Absence of AMH → Mullerian ducts persists
  - Absence of testost. → Wolffian ducts disappears (except ureteric bud)

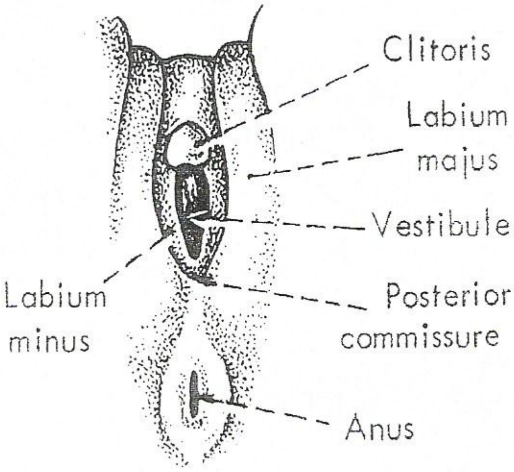
This means.......*femininity* is the NEUTRAL state & *masculinity* is the superimposed character ¤

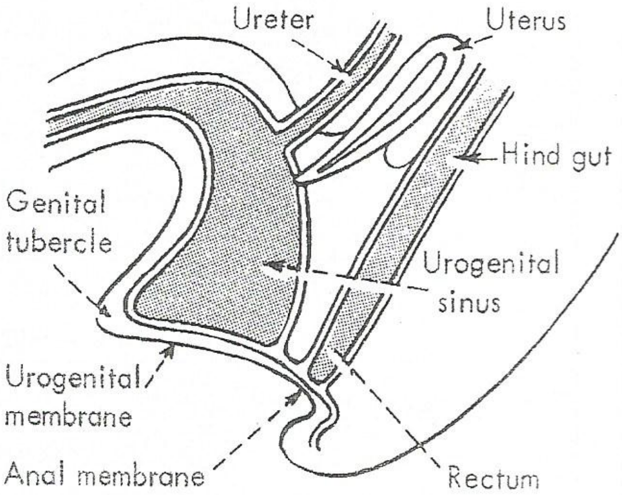
- **Further development**
  - Mullerian duct passes downwards & curves *medially* to fuse with the opposite duct in the midline. Then, *absorption* of the intervening septum will occur from below upwards
  - The *horizontal* unfused parts form ⟹ the fallopian tube
  - The *longitudinal* fused parts form ⟹ the uterus, cx, upper $\frac{4}{5}$ of the vagina
  - The lower end of Mullerian duct will project as a tubercle into the urogenital sinus to form a solid vaginal plate
  - Canalization of this plate (20wks) will form ⟹ lower ⅕ of the vagina
  - Junction between the *Mullerian duct & urogenital sinus* ⟹ the *hymen*

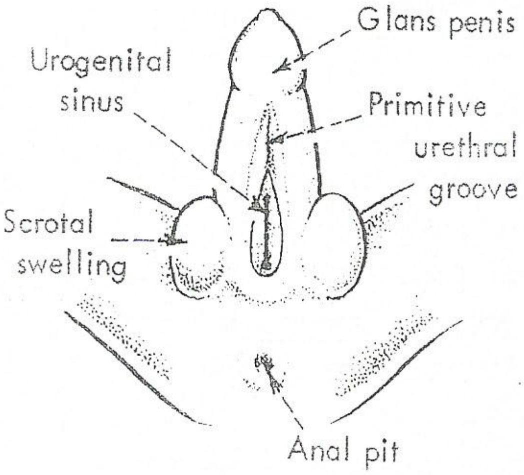

Allantois
Hind gut
Ureter
Cloaca


Genital
tubercle
Labial
swelling
Urogenital
membrane
Urethral
fold
Anal
membrane


Ureter
Cloacal
membrane
Uro-rectal
septum


Clitoris
Labium
majus
Vestibule
Labium
minus
Posterior
commissure
Anus


Ureter
Uterus
Hind gut
Genital
tubercle
Urogenital
sinus
Urogenital
membrane
Anal membrane
Rectum


Glans penis
Urogenital
sinus
Primitive
urethral
groove
Scrotal
swelling
Anal pit

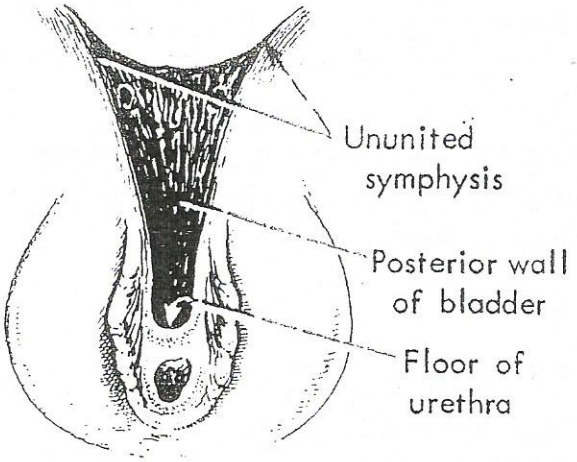
③ Development of the external genitalia

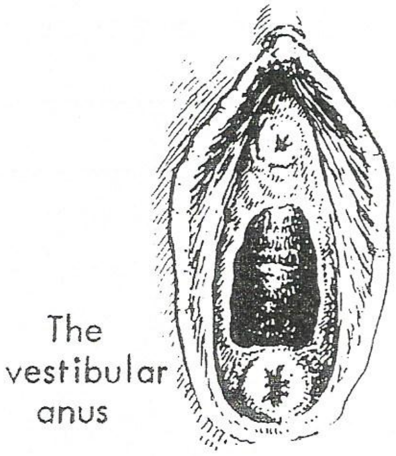
- **At outer surface of urogenital sinus:** 5 mesodermal swellings appear:
  1. The genital tubercle (phallus) ⇒ clitoris
  2. The TWO urogenital folds ⇒ labia minora
  3. The TWO genital (labio-scrotal) swellings ⇒ labia majora

- **Control**
  - IN MALES: Testosterone (by Leydig cells) → DHT (by 5α reductase of prostate) → masculinization (*enlargement & fusion*)
  - IN FEMALES: absence of testosterone → feminization

- **Cloaca**
  - The urorectal septum divides the cloaca (5-6 weeks) into
    . 2 compartments: rectum & urogenital sinus
    . 2 membranes: anal & urogenital membranes
  - The outmost part of the urogenital sinus forms → the vestibule

final products	Female ¤	Male ¤
Gonad	Ovary	Testis
Genital ridge	Infundibulopelvic lig. Ovarian lig., Round lig.	Gubernaculum
Mullerian duct (para-mesonephric)	Tubes, uterus, cx, Upper $\frac{4}{5}$ of vagina	Regress by MIF → remnants
Wolffian duct (mesonephric)	* All regresses except * ureteric buds & trigone	* Ureteric bud * Epididymis, ejac. duct
Cloaca: - *Urogenital Sinus* ¤ - *Anal canal*	. Lower ⅕ of the vagina . Hymen & Vestibule . Bartholin glands (greater vestibular gl.) . Urethra & paraurethral gl . Bladder → anus	. Prostatic utericle . Seminal colliculus . Cowper's glands (bulbo-urethral) . Urethra & prostate . Bladder → anus
Ext. genitalia ¤ 1] Genital tubercle 2] Genital fold 3] Gen. Swelling	 - Clitoris - Labia minora - Labia majora	 - Penis - Penile urethra (ventral) - Scrotum
kidney	*Pronephros* → *Mesonephros* → ***Metanephros*** (the permanent kidney ¤)	


Ununited
symphysis
Posterior wall
of bladder
Floor of
urethra


The
vestibular
anus

...... Congenital malformations ......

❶ External genitalia ΦΦ

- Ambiguous genitalia (intersex)
- Clitoris .Bifid......associated with ectopia vesica
  .Hypertrophy (clitromegaly)...isolated or part of generalized virilization
- Labial hypertrophy......dysparuenia or disfigurement → labial reduction
- Labial adhesions ¤......cong. or acquired✓✓ (infection or post-menopausal)
  TTT → simple surgical separation ± local estrogen ¤
- Vestibular anus

❷ Ovaries

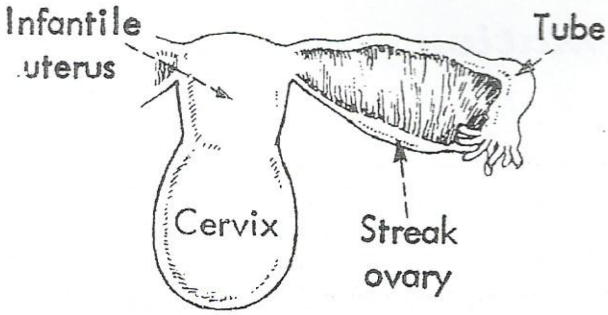
- Aplasia & hypoplasia
  - C/O → amenorrhea, infertility
  - Diagnosis → see amenorrhea
  - Treatment → HRT by cyclic E & P. pregnancy is impossible
- Dysgenetic ovaries e.g. Turner syndrome
  - C/O → 1^{ry} amenorrhea, no 2^{ry} sexual characters
  - Diagnosis:
    - * Phenotype → characteristic
    - * Karyotype → 45xo or mosaic: 45xo/46xx OR 45xo/46xy
    - * Ovaries → streak (fibrous) gonads
  - Treatment: HRT. Pregnancy is impossible
- Accessory (supernumerary) ovary → no complaint (found in br. lig.)
- Abnormal descent → very rare (the ovary found in high position)

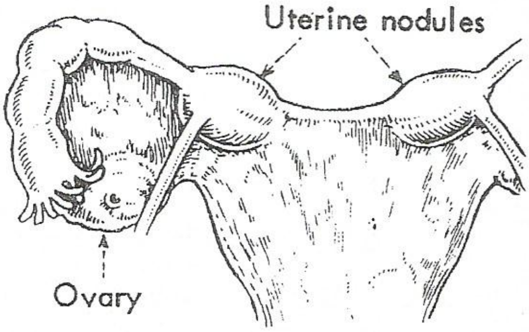
❸ Fallopian tubes

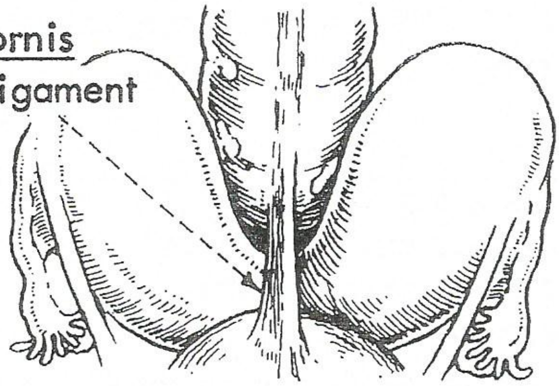
- **Aplasia** → infertility (± aplasia of uterus)
- **Hypoplasia** → short, tortuous, narrow → infertility, ectopic
- **Accessory ostia / diverticulum** → infertility, ectopic

❹ Cervix

- **Cervical atresia**
  - **C/O** → cryptomenorrhea & cyclic lower abdominal pain
  - **Diagnosis** → inability to introduce sound
  - **Treatment** → dilatation, If failed → hysterectomy !
- **Patulous internal os** ⇔ habitual abortion
- **Congenital elongation of portiovaginalis**
  - **C/O** → dyspareunia
  - **D.D.** → prolapse
  - **Treatment** → amputation if symptomatic





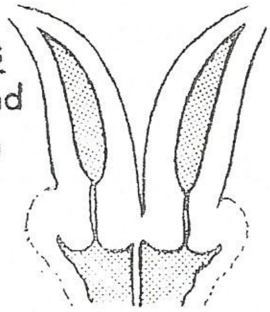


<u>Uterus Bicornis</u>

Note the ligament which usually passes from rectum to bladder.

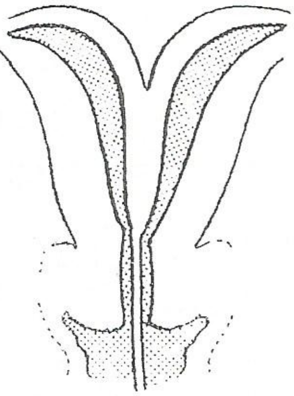
<u>Uterus Didelphys</u>

Double uterus and cervix, usually with double vagina.



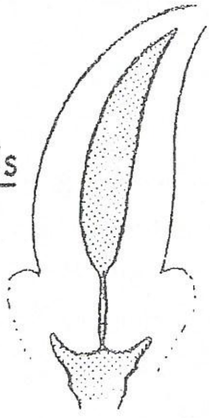
<u>Uterus Bicornis Bicollis</u>

Two corpora with fused cervices.



<u>Uterus Unicornis</u>

One duct has failed to develop.



⑤ Uterus

▸ **Aplasia:** 1^{ry} amenorrhea, infertility

▸ **Hypoplasia**

* **Types:** known by uterine index ⇨ CORPOREAL length / (CERVICAL length x 2)
  - *Rudimentary* (very small solid organ)
  - *Infantile* (body : cervix = 1 : 2)
  - *Pubescent* (body : cervix = 1 : 1)

* **C/O**
  - Amenorrhea or hypomenorrhea
  - Infertility or habitual abortion (in ascending manner)

* **Diagnosis of uterine diseases** ¤
  1. History
  2. Uterine sound
  3. Ultrasound (pregnant or non-pregnant)
  4. HSG / 5. Hysteroscopy / 6. Laparoscopy

* **Treatment**
  - Non-pregnant → cyclic E & P to ↑ uterine size.....
  - Pregnant → cerclage

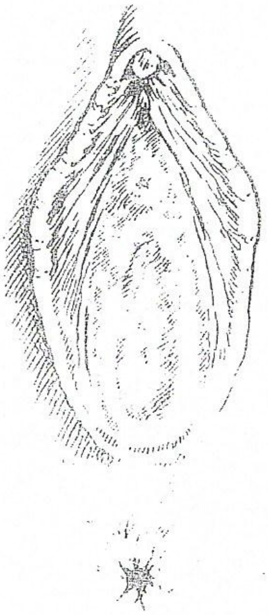
▸ **Fusion defects** Φ

1- **Uterus didelphys** ⇨ 2 bodies, 2 cervices, 2 vagina (vaginal septum)
2- **Uterus bicornis bicollis** ⇨ 2 bodies, 2 cervices
3- **Uterine bicornis unicollis** ⇨ 2 bodies, 1 cervix
4- **Septate & subseptate**
5- **Arcuate** (uterus cordiformis) a depression at the fundus
6- **Unicornuate** (complete arrest of development of one Mullerian duct)
7- **Rudimentary horn** (under-development of one Mullerian duct)
It may be *communicating* or *non-communicating* (blind horn)

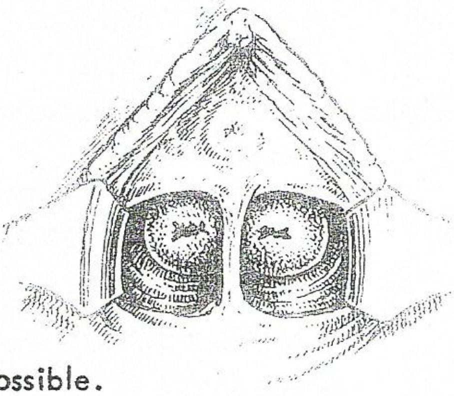
* **C/P**
  - Usually asymptomatic ✓; discovered accidentally or d.t. comp.
  - Spasmodic dysmenorrhea may be more common
  - Slightly ↑ menstrual flow (menorrhagia) in double uterus

* **Complications** ¤
  - **Early pregnancy**
    - Habitual abortion / PTL (abnormal shape & vascularity)
    - Ectopic pregnancy (in rudimentary horn)
  - **Late pregnancy** ⇨ malpresentations as transverse lie & breech
  - **Labor**
    - Obstructed labor (malpresentations)
    - Morbid adherence of the placenta (P.accreta) ¤

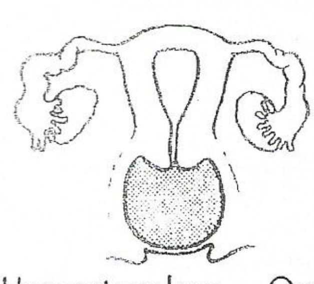
* **Treatment** ⇨ according to complaint and type of defect



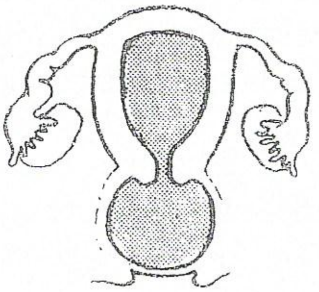
Complete absence of vagina. There is a slight depression over the hymen. Normal coitus is not possible.



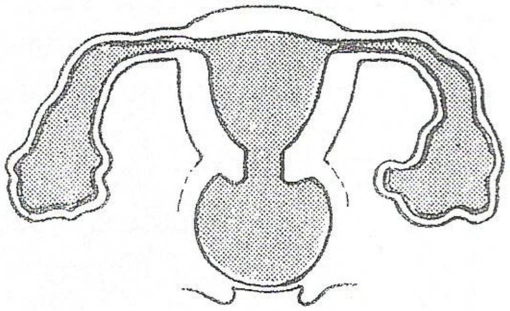
Septate (double) vagina showing also two cervices.
Normal pregnancy and delivery are possible.



Haematocolpos Only the vagina is distended by altered blood.



Haematometra The uterus is also distended.



Haematosalpinx In longstanding cases the tubes are also involved.

Imperforate hymen

⑥ Vagina

▸ **Vaginal aplasia**

- May be present alone OR
- More commonly with ✓ absent uterus ¤ → **Mullerian agenesis** ↲
  Mayer-Rokitansky-Kuster-Hauser syndrome
- *Renal* ¤ (30%) & *Skeletal* ¤ (15%) anomalies [IVP & X-ray is a must]

	Mullerian agenesis	Testicular feminization $
Etiology	congenital anomaly	insensitivity to androgens
Karyotype	46xx	46xy
Phenotype	normal ♀	normal ♀ (tall + no hair))
Gonad	ovary	testis
Hormones	estrogen	♂ level androgen
Int. genitalia	------------	------------
Ext. genitalia	vaginal pouch	vaginal pouch

- Treatment
  1. Frank method → use of progressive dilators
  2. Vaginoplasty →
     . McIndoe's operation: dissection bet. bladder & rectum
     . William's operation: creation of a labial pouch
  3. Abdominal → colon vaginoplasty ± skin graft or amnion graft
  4. Laparoscopic → Vachetti operation (gradual traction of a ball)

▸ **Longitudinal vaginal septum** (± duplication of uterus)

- **C/O** → asymptomatic **or** may lead to dyspareunia **or** obstructed labor if breech overrides septum during breech delivery

▸ **Transverse vaginal septum**

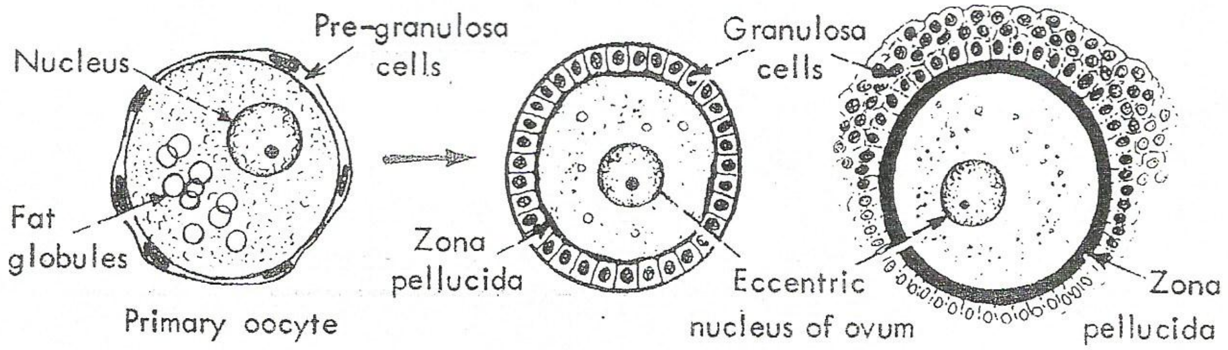
- Upper → between the upper & middle ⅓ of the vagina
- Lower → site of fusion bet. Mull. ducts & urogenital sinus
  – upper $\frac{4}{5}$ & lower ⅕ –

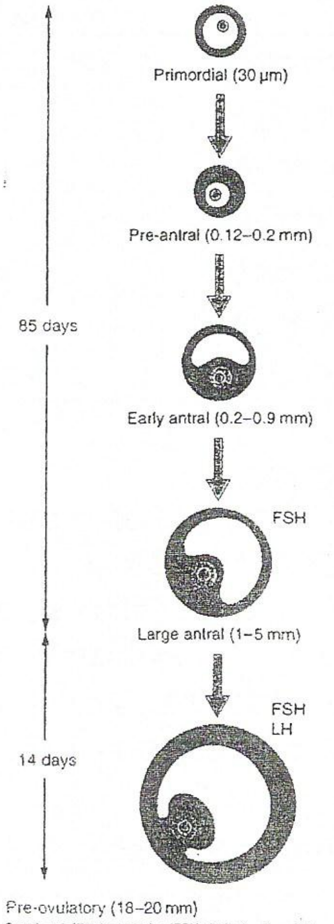
▸ **Imperforate Hymen** ✓✓⬭⬭

- Due to → failure of complete canalization of the vaginal plate
- Leading → to cryptomenorrhea = false amenorrhea

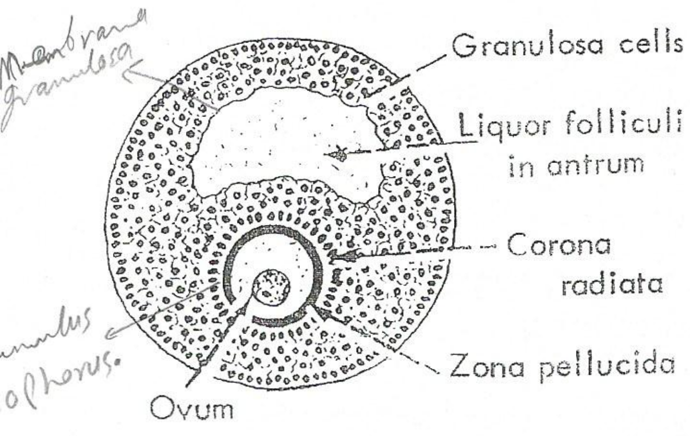
NB.....imperforate hymen is bluish & bulging than tr vag septum (thick)

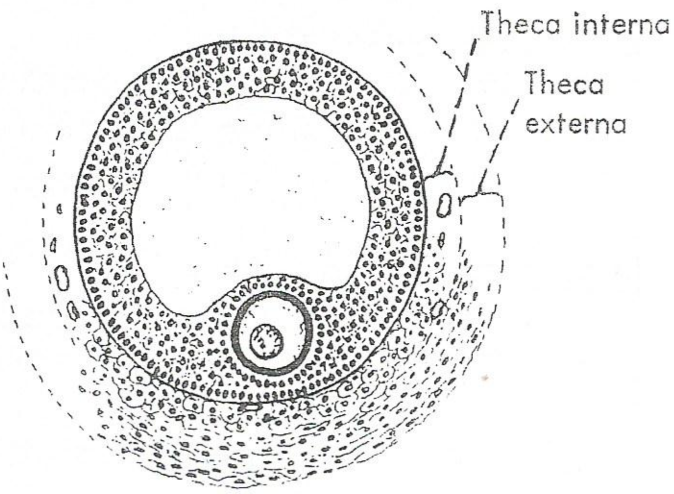
▸ **Congenital Vesicovaginal or Rectovaginal Fistula**





Ovarian folliculogenesis. (FSH, follicle-stimulating hormone; LH, luteinizing hormone.)





Physiology

Menstrual Cycle

Ovarian cycle

❶ Follicular phase: 1-13 day

▸ **Primordial follicle** (50μ)

- Over 400–1000 primitive oocytes enter growth phase / cycle
- Each one is surrounded by single layer of granulosa cells ↳ arrested in *prophase* of *1st meiotic* division ¤

▸ **Preantral follicle** (200μ)

- FSH stimulates follicular growth → oocytes become surrounded by several layers of granulosa cells → ↑ 'E' production → ↑ more FSH receptors → more follicular growth (vicious cycle)
- Granulosa cells can't produce E alone

The Two cell theory
* LH → stimulates 'androgen' in <u>*theca*</u> cells
* FSH → stimulates 'estrogen' in <u>*granulosa*</u> (by aromatization of An from theca cells)

▸ **Antral follicle**

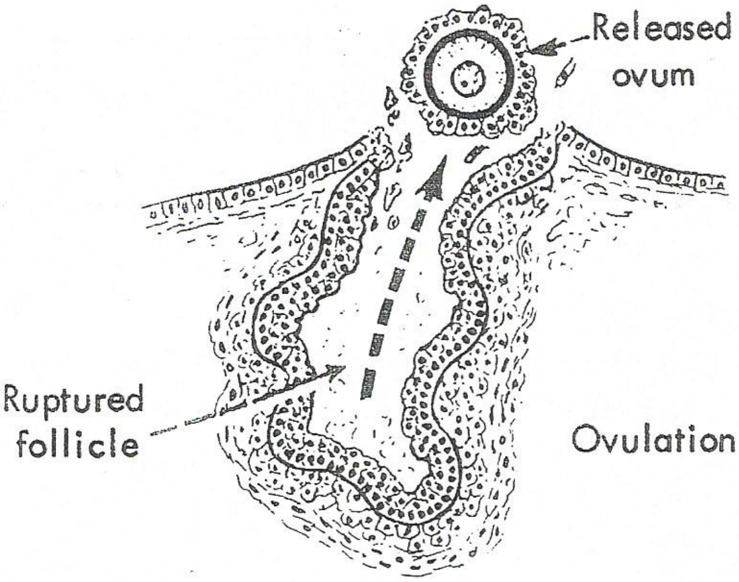
- Multiple fluid spaces between granulosa cells join together to form a large *antrum* full of "E'. This high 'E' (± inhibin) → ↓ FSH → ↓ aromatization → ↑ local androgen → atresia of most follicles → ↓ action of G. cells
- The antral follicle (**the dominant follicle**) → by day 7 is immune against this atresia as it has large number of FSH receptors ¤

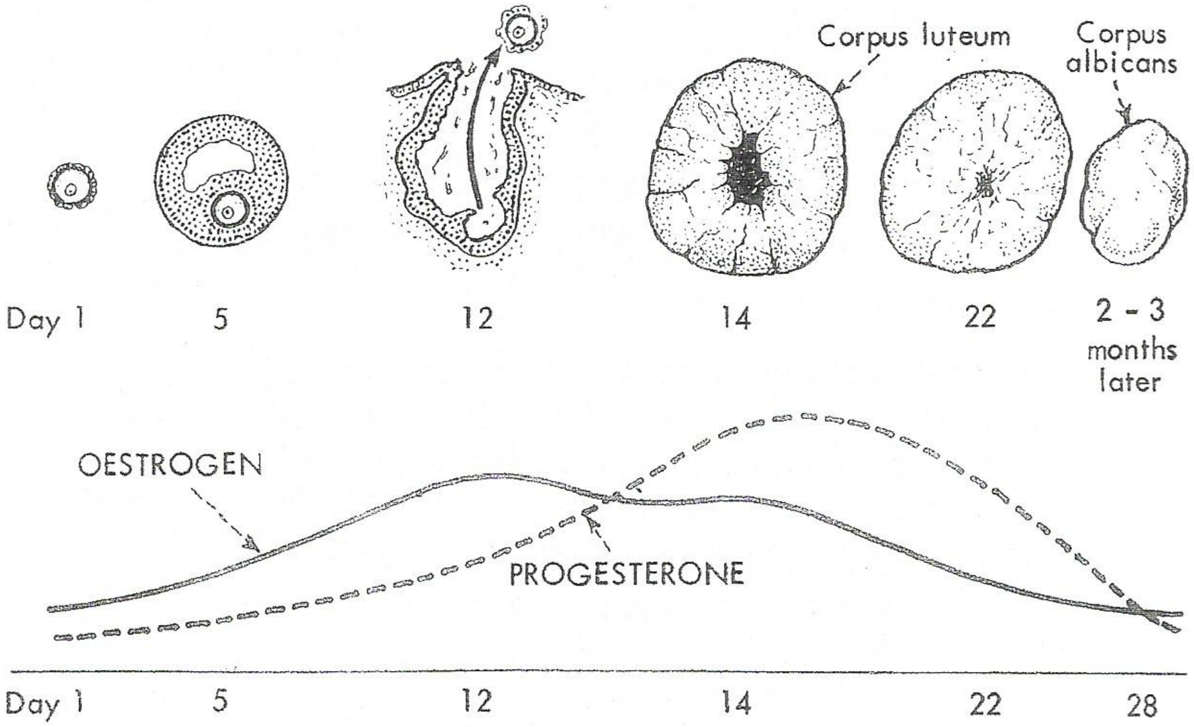
▸ **Preovulatory follicle** (18–24mm ¤)

- Here, the oocyte resumes the prophase of meiosis I ↳ haploid (½) no of chromosomes + 1st polar body
- Meiosis II (mitotic like) occurs upon fertilization ↳ 2ry oocyte & 2nd polar body
- Layers of **mature Graafian follicle**
  - *Ovum*……………*Perivitelline space*…………*Zona pellucida*
  - *Corona radiata*……*Cumulus Oophorus*……*Antrum folliculi*
  - *Membrana granulosa*…..*Theca interna*………*Theca externa*

Functions of LH:

1. Production of Androgen → ↑Libido
   ↘ Atresia of nondominant follicles
2. — —
3. Ovulation.
4. formation of CL.





ليه الست الحامل مجيلهاش دورة؟ . علشان E, P مبينزلوش.

❷ Ovulation: 13-15 "the fertile phase"

- When E ↑ > 200 pg/ml for > 50 hrs → +ve feedback on LH
  - **LH surge** → ovulation within 36 hours ¤
  - There is also a **smaller FSH surge (2nd surge)** ¤
    - to ↑ LH receptors in the follicles.
- LH stimulates **androgen** production theca cells to:
  - Ensure complete atresia of the non-dominant follicles
  - Increase libido at midcycle
  - Production of PG → Cont. of ovarian smooth ms → Release of ovum.
- **Extrusion** of the ovum m.b.d.t. (Theories)
  - Proteolytic enzymes (collagenase, hyaluronidase) → stimulated by LH
  - Contraction of ovarian smooth muscle (by PG) → stimulated by androgen + LH
  - Pressure effect of the antrum folliculi
- The midcyclic ↑ in LH is **short-lived** d.t.
  - Exhaustion of the LH storage in the pituitary
  - Loss of the +ve feedback stimulus of E (due to ↓ E)
  - -ve feedback on hypothalamus → ↓ GnRH.

❸ Luteal phase: 14 days

CL reaches maximum at day 21 (after 7 days).

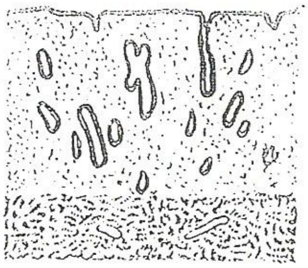
- **CL formation**
  1] **Proliferative stage** ⇨ 'G' & 'T' cells multiply rapidly
  2] **Luteinization stage** ⇨ deposition of cholesterol → yellow vacuolated cells → steroidogenesis → E & P (peaks within a week i.e. day 21)
    - *Granulosa cells* → lutein cells
    - *Theca cells* → paralutein cells
    - (Both produce E + P)
  3] **Vascularization** (mature CL) ⇨ the most vascular organ in the body in relation to its size.

- **Fate of CL**
  4] **IF NO PREGNANCY** ⇨ **Retrogression:**
    E & P from CL → –ve feedback on LH & FSH
    → CL starts degeneration at the 22nd day
    → Corpus albicans → corpus fibrosum
    → ↓ E & P → menses + release of –ve inhibition on LH & FSH
    → ↑ LH & FSH → start of a new cycle

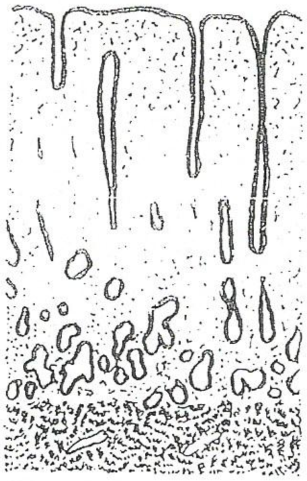
  5] **IF PREGNANCY OCCURS** ⇨ **CL of pregnancy:**
    trophoblast → HCG → stimulates more growth of CL (hypertrophic, larger, cystic) → maintenance of high E & P till 12 wks (till placenta forms)

$PGf_{2}\alpha \rightarrow$ V.C.
$PGE_{2} \rightarrow$ V.D

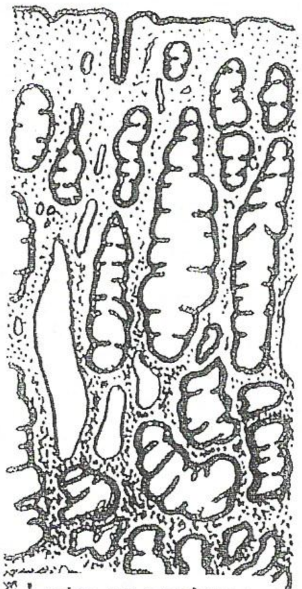
$PGf_{2}\alpha \rightarrow$ formed depending on P.
Ischemic pain before menses [illegible]
1- sign for P. production → sign for ovulation.
* for relief of that pain → use Anti- PG. agent. (↓ $PGf_{2}\alpha$)



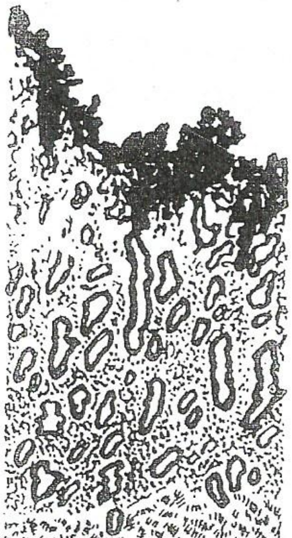
Early proliferative phase



Late proliferative phase



Late secretory phase



Menstruation

Endometrial Cycle

* 4 Phases ▼

	❶ Regeneration	❷ Proliferative	❸ Secretory
Origin	from basal glands	E effect from follicles	P + E from Corpus luteum
Duration	1-2 days	9-10 days	14 days – fixed period –
Thickness	1-2 mm	3-4 mm	7-8 mm
Epithelium	Cuboidal ciliated	columnar	High columnar + secretions appear in vesicles (1st they appear subnuclear → then become supra-nuclear)
Glands	Simple, Tubular, Narrow	↑ in number Elongated Dilated	Tortuous (corkscrew & Saw-tooth appearance) + secretions distend lumen
Stroma	Few	increased cellularity	↑size of cells,stromal edema + leukocyte infiltration
Vessels	Few	↑ed ($PGF_{2\alpha}$ = PGE_2)	Basal +spiral (↑ $PGF_{2\alpha}$)

* **Functional layers of endometrium**

- Superficial (⅔)……H. sensitive, contain spiral arteries –end arteries–
- Basal (⅓)…………H. resistant, contain basal arteries –for regeneration–

* **Histological layers of endometrium**

- Stratum basalis……….(around gland bases)…...¼ thickness
- Stratum spongiozum…(around gland bodies)….½ thickness
- Stratum compactum…(around gland necks)….. ¼ thickness

❹ Menstrual phase

♣ Degeneration of CL ➟ **withdrawal of progesterone:**

- Shrinkage of endomet. & ⇩ edema → coiling of spiral arteries (up to 8 loops)
- Breakdown of lysosomes → $PGF_{2\alpha}$ → VC & myometrial contraction
- This leads to severe ischemia of spiral vessels for 4–24 hrs
  ↳ necrosis only of strata compacta & spongioza → shedding of endometrium + opening of vessels follows → massive blood loss

♣ Menstrual blood ➟ **stops due to:**

- Vasoconstriction (mainly) & haemostatic plug formation
- Regeneration from zona basalis (protected from the monthly shedding as it is supplied by the basal arterioles)

★ How to stop bleeding? → venostatics mainly.

1- Try hemostatics (Daflon, Dicynone) → usually not effective (menstrual blood is 75% arterial + 25% venous).

2- Hormonal therapy (E+P): ↑ $PGF_{2\alpha}$ → V.C → ↓ bleeding.

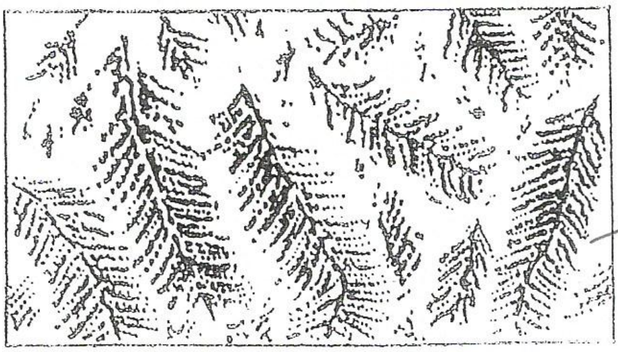
3- Hysterectomy.

★ How to measure the amount of blood?

1- Direct → using cervical cap.

2- Indirect → measuring occult Hb in napkin.

أجيب الـ napkins وعليها bleeding من مريضة ← تشرب الدم اللي فيها وبعد كده أقيس نسبة الـ Hb



→ precipitation of NaCl, KCl

'Ferning' pattern in vaginal smear due to oestrogen stimulation.

Signs of ovulation.

I- History: 1- Regular cycles. 2- Pain before menses. 3- midcycle discharge.

II- Ex.

III- Inv: 1- P. at day 21. 2- End. biopsy at day 21.

★ Vaginal smear:

1- Intermediate cells only → P. → Preg.

2- Superficial cells only → E. → follicular stage.

3- Basal cells only → No E., No P. → postmenopausal.

⌘ *Normal menstruation* ☠ ☠

- **Rhythm** ⇨ regular every 21–35 days
  (<21 =polymenorrhea, >35 =oligomenorrhea)
- **Duration** ⇨ average 3-5 days
  (<2 =hypomenorrhea, >7 =menorrhagia)
- **Amount** ⇨ 50–80 cc: average 3 napkins /day
  (<30 =hypomenorrhea, >80 =menorrhagia)
- **Composition** ⇨ blood, endometrial shreds, FDPs, leukocytes, cervical mucous, desquamated vaginal epithelium, bacteria
  ⇨ Normally 75% *arterial* blood & 25% *venous* blood

- Normally menstrual shedding forms clots inside the uterine cavity ➟ fibrinolysis ∴ it pass outside as **fluidy blood**
- In cases of severe bleeding ➟ **blood clots** ✓ (bleeding exceeds capacity of fibrinolytic system) + **colicky pain**

Cervical cycle

	Follicular phase.........(E_2) maximum at ovulation time ¤	**Luteal phase.......(P.)** max 1 wk after ovulation ¤
Discharge	excessive watery (copious)	scanty viscid (dry)
Fern (if mucous is left to dry)	+ve (↑ electrolytes: NaCl, KCl)	–ve (no-arborization)
Spinnbarkeit (stretchebility bet. 2 slides)	+ve (stretchable up to 10 cm)	–ve (non-stretchable) viscid, thick

Vaginal cycle

Studied by vaginal smear (exfoliative cytology) from posterior fornix ς maturation (cornification) index → denotes the hormonal state

Follicular phase.........(E_2)	**Luteal phase.........(P.)**
. Superficial cells (polygonal)	. Intermediate cells (navicular)
. Acidophilic cytoplasm	. Basophilic cytoplasm
. Pyknotic nucleus (small, dark) + few leukocytes	. Clear (vesicular nuclei) + many leukocytes

Both E. and P. stimulates prolactin release but blocks its effect.
Appearance of milk in preg. → suspect for IUFD

Hormones :

❶ Estrogens [C-18 steroids]

▸ Types

- Estradiol (E_2) → most potent, most important
- Estrone (E_1) → less potent, estrogen of menopause
- Estriol (E_3) → least potent, very high levels in pregnancy
- Estetrol (E_4) → very weak, ♀ fetus.

▸ Source * **Glands** ⇨ ovary (GF✓✓ + CL), placenta, suprarenal cortex
* **Peripheral conversion** ⇨ of androgens (30% of Є) cholesterol → P. → and. → E.

▸ **Metabolism:** 99% bound (SHBG)… metabolized in liver

▸ Actions Φ

-1- General – (anabolic & proliferation)

* **Metabolic**
  - **Protein** → anabolic with nitrogen retention +ve nitrogen balance.
  - **Lipid** → protective effect against IHD (↑ HDL + ↓ LDL)
  - **CHO** → some anti-insulin action
  - **Coagulation** → ↑ thrombosis (↑ clotting factors + ↓ fibrinolysis)
* **Bone** ⇨ stimulates osteoblastic activity → growth spurt then closure of the epiphysis. But it still protects against osteoporosis.
* **Endocrinal system**
  - **Pituitary gland:** -ve feedback on FSH, +ve on LH → ovulation (if 200 pg/ml for 50 h.)
  - **Breasts:** Stimulates duct system mainly + ↑ vascularity + ↑ fat
    In pregnancy → ↑ prolactin release but blocks its action
  - **Increases all binding globulins** (SHBG, TBG, CBG)

-2- Local – (esp at puberty & pregnancy)

* **Vulva & vagina** ⇨
  - Increase vascularity, size + deposition of fat
  - More deposition of glycogen → lactobacillus Doderlines
* **Cervix** ⇨ secretion becomes fluidy, alkaline → +ve Spinb. & Fern
* **Uterus** ⇨ proliferation & hyperplasia + ↑ vascularity + ↑ β receptors.
* **Tube** ⇨ ↑ vascularity, hypertrophy of muscles + ↑ peristalsis

▸ Uses Φ

1] **Contraception** ⟹ e.g. in contraceptive pills
2] **Infertility** ⟹ to improve pattern of cervical mucous
3] **Infections** ⟹ to improve healing (postmenop., trophic ulcer, vulval dystrophy)
4] **Menstrual disturbances** ⟹ DUB, dysmenorrhea
5] **Menopause** ⟹ ERT (Estrogen Replacement Therapy)

❷ Progesterone [C-21 steroids]

▸ Types

1) ***Natural progesterone***....utrogestan, duphoston
2) ***Synthetic***
   - ◆ 1st generation
     - *ESTRANE* → **Nor**ethindrone, **Nor**esthisterone, **Nor**gestrel
     - *PREGNANE* → Medroxy progesterone acetate
   - ◆ 2nd generation: Levonorgestrel
   - ◆ 3rd generation: (new progestins) = ↑ potency + ↓ androgenic effects
     Desogestrel (*Marvelon*) – **Gest**odene (*Gynera*) – Norge**st**imate (*Cilest*)

▸ Source ⇨ Ovary (CL✓✓), placenta, suprarenal glands

▸ Metabolism ⇨ *bound* to SHBG… *metabolized* in liver (pregnandiol ¤)
↳ metabolite of P. in urine.

▸ Actions Φ

-1- General -- anti-estrogen

- Thermogenic (increased BBT)
- Stimulates respiration (esp in pregnancy)..depth & not rate
- Relaxes smooth muscles (e.g. GIT & ureter)
- Salt & water loss ¤
- **Breast** → stimulates alveolar ¤ system development in breast
  (but blocks the action of prolactin during pregnancy)
- **Pituitary** → -ve feedback on FSH & LH → inhibition of ovulation

-2- Local -- prepare for pregnancy

* **Vagina** ↓ thickness & ↓ acidity of epithelium
↓ maturation (increased intermediate folded basophilic cells)

* **Cervix** ↓ secretions → viscid & cellular with -ve Spinb. & Fern test

* **Uterus**

- **Endometrium** → .changes from proliferative → secretory
  .In pregnancy→ decidua. . .Prolonged use→ atrophy (at least 9m.)
- **Myometrium** → hypertrophy & decreased tone & motility
  (↓ sensitivity of pregnant uterus to oxytocin) Recently used as tocolytic.

* **Tubes** → decreased motility

▸ Uses Φ

Obstetrics	Gynecology (Anti-estrogen)	± Estrogen in
- Threatened abortion - C. luteum insufficiency - Habitual abortion - Surgery during pregnancy	- Endometriosis - Endomet. hyperplasia - Endometrial carcinoma	- HRT, some amenorrhea cases - DUB (dysfunctional ut. Bleeding) - PMT (Premenstrual tension) - COC (Contraceptive pills)

❸ Androgens [C-19 steroids]

▸ Types & sources

OVARY		ADRENAL
25 %	Testosterone	25 %
50 %	↻ Androstenedione ↺	50 %
10 %	DHEA	90 %
0 %	DHEA-S	100 %

▸ Metabolism

- Bound (99%) to SHBG & albumin……1% free
- 'T' (in hair follicle) → 5α-reductase → DHT (dihydro-testosterone)

▸ Action

- Normally the level is too low to cause any effect (axillary & pubic hair, normal female libido)
- But it may increase (e.g. PCO & androgen producing tumors) ⤸
  - Anovulation & infertility
  - Hirsutism
  - Defeminization followed by → virilization

▸ Uses ✗✗ (not preferred at all)…….but may be used in

- Vulval dystrophies (atrophic types)
- Some sexual disorders (↓ed libido ✓✓)

Anatomy of the pituitary gland

- Lies in the sella turcica
- Covered by diaphragma sellae → pierced by the pituitary stalk (carries vessels & nerves from hypothalamus to pituitary)
- Lies behind the optic chiasma ¤
- On each side → the cavernous sinus
- Below it → the sphenoid bone

Parts of the pituitary gland

	Ant. lobe (adeno-hypophysis)			Post. lobe (neuro-hypophysis)
Origin	Rathke's pouch (upper part of pharynx) ¤			Down growth from dienceph.
Control by	Portal circulation ¤			Nerve fibres ¤
Hormones	Acidophil	Basophil	Chromophobe	- Oxytocin & ADH
	- GH - PRL	FSH + LH TSH ACTH	- Reserve cells - May release PRL	- Formed in hypothalamus - Pass along axons in stalk - Stored & released from pit.

The Gonadotrophins (FSH, LH, HCG)

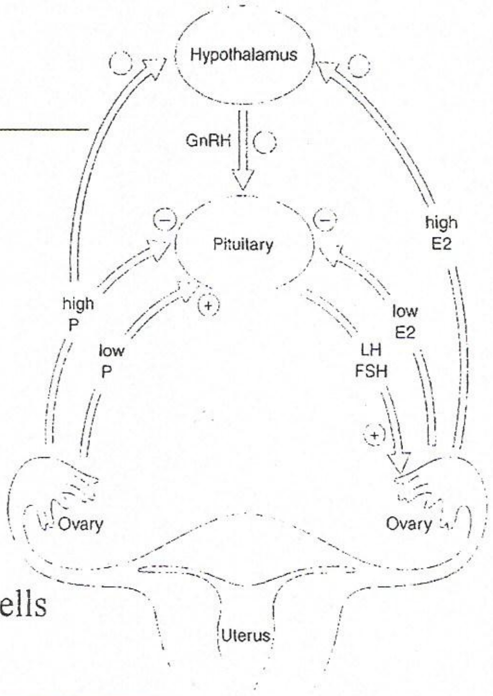
▸ **Source**

- **FSH, LH** are secreted by the anterior pituitary (**basophils**) ¤
- **HCG** is secreted by *trophoblast* (also produces some FSH & LH ¤)
- They pass to blood free (unbound) as they are released in little amounts ¤

▸ **Chemistry**

- They are all **glycopeptides** ¤ having similar α-chains, different β-chains
- So in cases of assay of HCG we do β-subunit assay

▸ **Actions** Φ



--FSH--

- Stimulates development of follicles
- Increases FSH & LH receptors
- Stimulates steroidogenesis in granulosa cells
- FSH surge ¤ is important to stimulate formation of LH receptors
- Control is by → -ve feedback by E & P (through inhibin)

--LH--

- LH surge causes ovulation
- Stimulates steroidogenesis by theca cells
- Responsible for luteinization of theca & granulosa cells

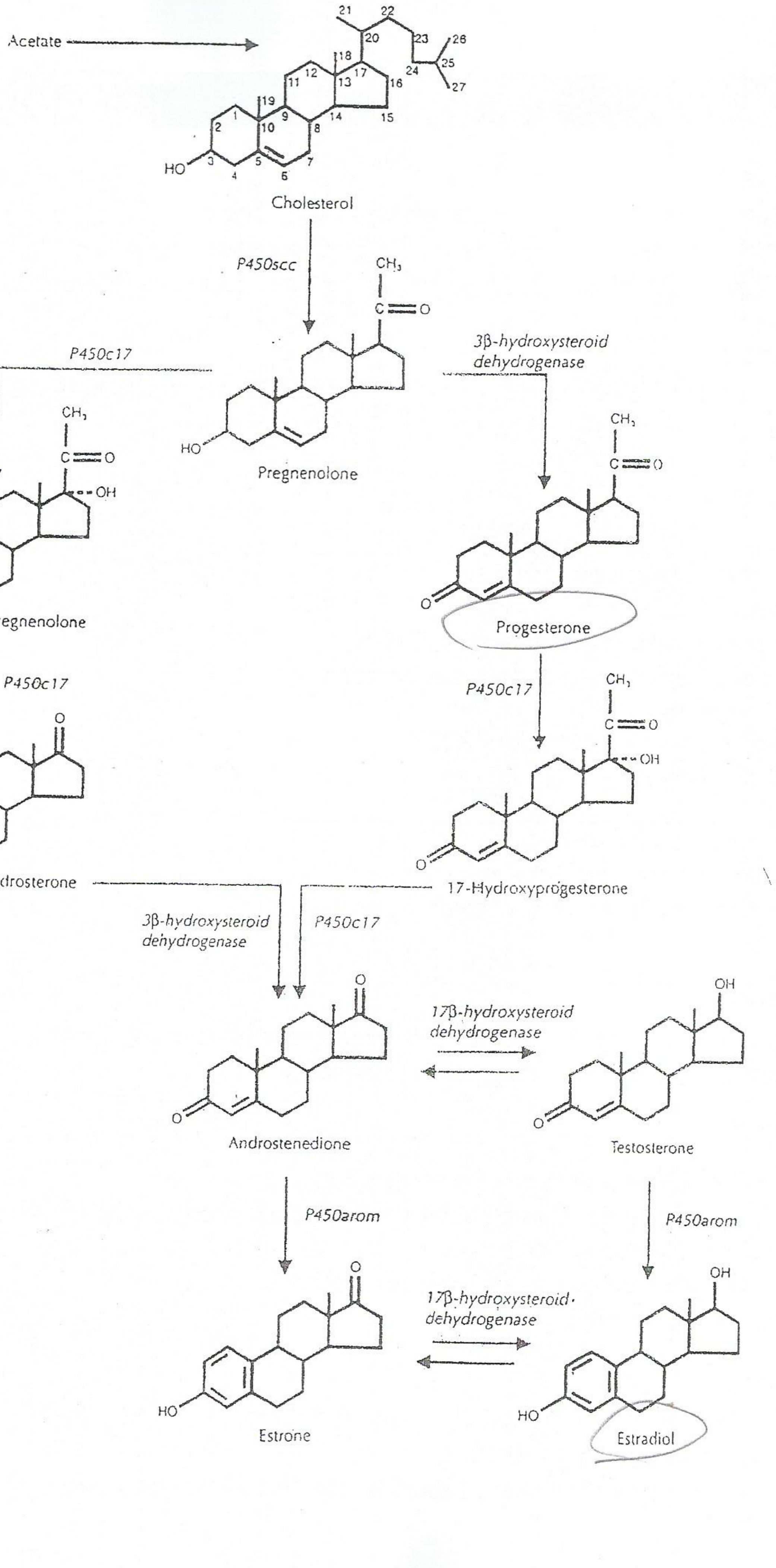
--HCG--

- Similar to LH ¤
- Maintains CL in preg. till placental steroidogenesis is sufficient (>12 wk)
- Important for proper spermatogenesis in male fetus ¤

▸ **Uses** Φ

- *FSH & LH* ➡ induction of ovulation in:
  - Hypothalamic *failure*, pituitary *failure*, clomiphene induction *failure*
  - Unexplained infertility
  - Assisted reproductive techniques (ART)
  - Male infertility

- *HCG* ➡
  - Ovulation (LH like activity) given as 5.000 – 10.000 IU / IM
  - Corpus luteum insufficiency
  - Some cases of threatened abortion (instead of progesterone)


Acetate
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2
10
8
3
5
7
HO
4
6
Cholesterol
P450scc
CH3
C=O
3β-hydroxysteroid
dehydrogenase
P450c17
HO
Pregnenolone
CH3
C=O
OH
CH3
C=O
HO
17-Hydroxypregnenolone
O
Progesterone
P450c17
P450c17
CH3
O
C=O
OH
HO
Dehydroepiandrosterone
O
17-Hydroxyprogesterone
3β-hydroxysteroid
dehydrogenase
P450c17
O
OH
17β-hydroxysteroid
dehydrogenase
O
O
Androstenedione
Testosterone
P450arom
P450arom
O
OH
17β-hydroxysteroid
dehydrogenase
HO
HO
Estrone
Estradiol

Gonadotrophin Releasing Hormone (GnRH)

▸ Function

- GnRH (previously LHRH) is a *decapeptide* which stimulates
  - Synthesis & storage of Gn (reserve pool)
  - Induce immediate release of gonadotropins (releasable pool)
- GnRH is released in pulsatile fashion (every hour)

▸ Control

❶ **Negative feedback loops** ¤

- Long feedback loop by ovarian steroids
- Short feedback loop by Gn
- Ultrashort feedback loop: GnRH inhibit its own release

❷ **Neurotransmitter control on the Hypothalamus**

- Noradrenaline → ↑ GnRH
- Dopamine, serotonin, β-endorphins → ↓ GnRH

▸ Uses of GnRH analogues Φ

- Nasal spray ⇨ Nafarelin (synarel).... Buserelin (superfact)
- SC injection ⇨ Goserelin (zoladex)
- IM injection ⇨ Triptorelin (decapeptyl).....Leuprolide (lupron)

1) **If used in pulsatile manner** ¤

ç induction of ovulation (with no risk of OHSS ¤)

2) **If used in continuous manner**

* Down regulation of pituitary receptors → inhibition of FSH & LH → ↓ E (medical castration) ∴ used for

- *Superovulation* → ART
- *Contraception*
- *Some 'E' dependant tumors: fibroids, end. hyperplasia, EØ*
- *Dysfunctional uterine bleeding*
- *Idiopathic precocious puberty.....Idiopathic hirsutism*

* So main side effect is → pseudo–menopausal state esp *Osteoporosis* ∴ ADD BACK THERAPY of "E + P" may be given ¤

Normal Hormonal levels

	Follicular phase	Luteal phase
Estrogen	30-75 pg/ml	200-300 pg/ ml
Progesterone	< 1 ng/ml	>12 ng/ml
Testosterone	0.2–0.8 ng/ml	
Gonadotrophin	FSH → 5-30 mIU/ml LH → 5-20 mIU/ml	
Prolactin	2–20 ng/ml	

Chapter 2 Endocrinology

Puberty

Menopause

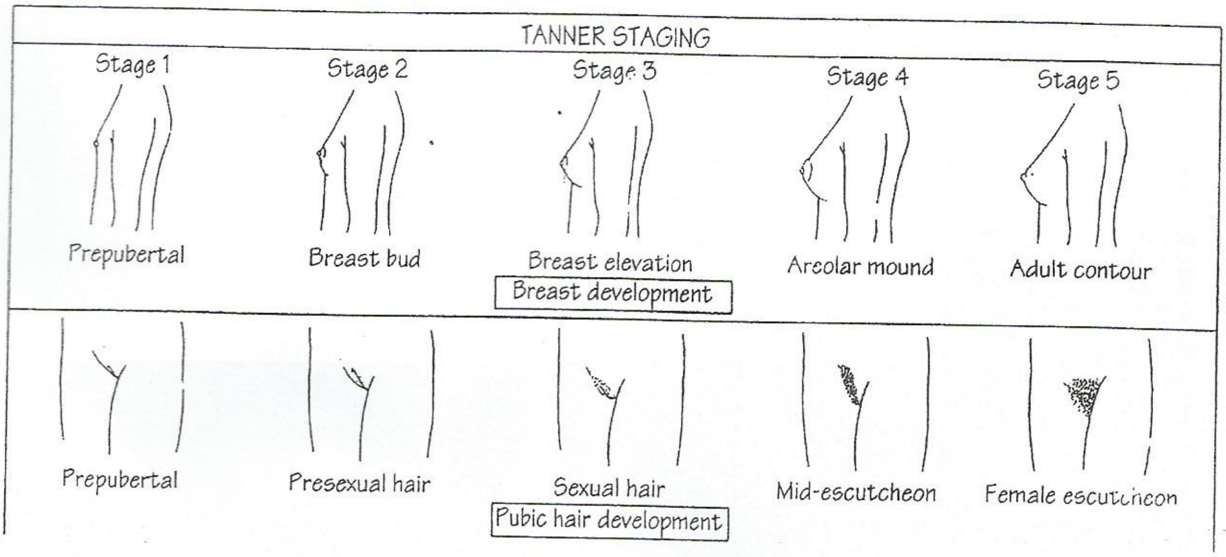
Amenorrhea

Anovulation-PCO

Abormal bleeding

Dysmenorrhea

Importance of Androgens in ♀:
1- ↑ libido at midcycle (Time of ovulation).
2- ↑ hair growth (pubic and axillary.



TANNER CLASSIFICATION

		Breast	Pubic hair
1	Pre-pub	elevated breast papillae (مفيش حاجة)	Not present (مفيش)
2	10 yrs	Breast bud → small mound (ارتفاع صغير)	Sparse on labia majora (شعر خفيف)
3	11 yrs	Further enlargement (round & small)	Darker, coarser, curled (شعر تقيل)
4	12 yrs	2^{ry} mound (areola project out)	Also on mons pubis (طلع لفوق)
5	14 yrs	Adult contour (2^{ry} mound disappear)	Also on medial thigh (راح للجنب)

Puberty

Definition

. ~~Age~~ of transition from **childhood** to **adulthood** physically ending in full **sexual** & **reproductive** development

. Puberty is a *period* of time (8–13 yr), menarche is an *event* (12 yr)

Before puberty

- There is no / very little 'E' secreted due to:
  - GnRH suppression (unknown, mostly controlled by a gene in GnRH nucleus)
  - Very sensitive HPO axis to –ve feedback of steroids
- Variation of age of start of puberty is due to several factors: e.g.
  - Constitutional, genetic predisposition
  - Psychological factors
  - Nutrition, activity (athletes have later puberty)
  - Melatonin release from pineal glands

Normal puberty

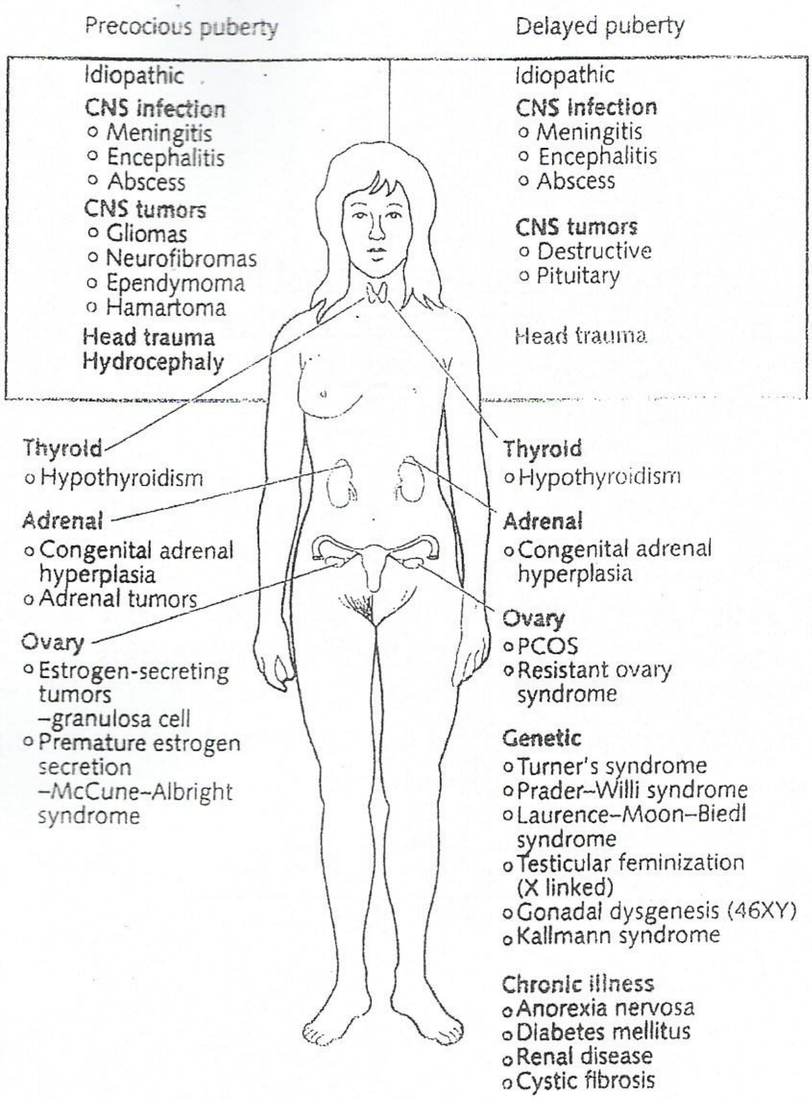
. It takes a period of time → 2–5 yr

. Girls reach puberty → ± 2 years < boys

1. **Somatic changes**
   - Growth spurt ✓✓ [peaks at 11 yr]...followed by → closure of epiphysis
   - Deposition of fat → feminine round contour
   - Persistence of high pitched voice

2. **Secondary sexual characters**
   - *Gonadarche* ➨ the initial release of LH & FSH
   - *Thelarche* ➨ first appearance of breast buds.........the 1st event
   - *Adrenarche* ➨ activation of adrenal androgens
     (*Pubarche*)(full appearance of axillary & pubic hair)
   - *Menarche* ➨ occurs 2 yr after onset of breast........the last event
     ς initial cycles are usually anovulatory

3. **Genital changes** (d.t. ↑ E) ......development of the reproductive organs


Precocious puberty
Idiopathic
CNS infection
o Meningitis
o Encephalitis
o Abscess
CNS tumors
o Gliomas
o Neurofibromas
o Ependymoma
o Hamartoma
Head trauma
Hydrocephaly
Thyroid
o Hypothyroidism
Adrenal
o Congenital adrenal hyperplasia
o Adrenal tumors
Ovary
o Estrogen-secreting tumors
–granulosa cell
o Premature estrogen secretion
–McCune–Albright syndrome
Delayed puberty
Idiopathic
CNS infection
o Meningitis
o Encephalitis
o Abscess
CNS tumors
o Destructive
o Pituitary
Head trauma
Thyroid
o Hypothyroidism
Adrenal
o Congenital adrenal hyperplasia
Ovary
o PCOS
o Resistant ovary syndrome
Genetic
o Turner's syndrome
o Prader–Willi syndrome
o Laurence–Moon–Biedl syndrome
o Testicular feminization (X linked)
o Gonadal dysgenesis (46XY)
o Kallmann syndrome
Chronic illness
o Anorexia nervosa
o Diabetes mellitus
o Renal disease
o Cystic fibrosis

Abnormal puberty /adolescence / child-hood

- *Congenital* ⇨ ambiguous genitalia (intersex)
- *Traumatic* ⇨ circumcision…sexual abuse…accidental trauma (FB)
- *Inflammatory* ⇨ prepubertal vulvovaginitis ✓✓
- *Neoplastic* ⇨ ovary (germ cell tumor), vagina (sarcoma botryoids)
- *Miscellaneous* ⇨
  - Early (precocious) / Delayed Puberty
  - Menorrhagia (1st exclude coagulopathy)
  - Dysmenorrhea

Q. The commonest pre-pubertal gyn. **complaint**? discharge (V.Vaginitis)

Q. The commonest pre-pubertal gyn. **bleeding**? F. body / severe V.Vaginitis

Q. What are the indications of P/R in gynecology?

- **Virgins** ✓✓
- **Congenital** → imperforate hymen
- **Traumatic** → . complete *perineal tears & fistula*
  . differentiates *rectocele* from *enterocele*
- **Neoplastic** → -routine in all tumors e.g. cancer cervix
  -masses in D. pouch e.g. endometrioma
- **Miscellaneous** → Bleeding / rectum

① *Delayed puberty*

Definition

- No menarche by 16
- No secondary sexual characters by 14
- No menarche for 5 years after completed thelarche

Etiology

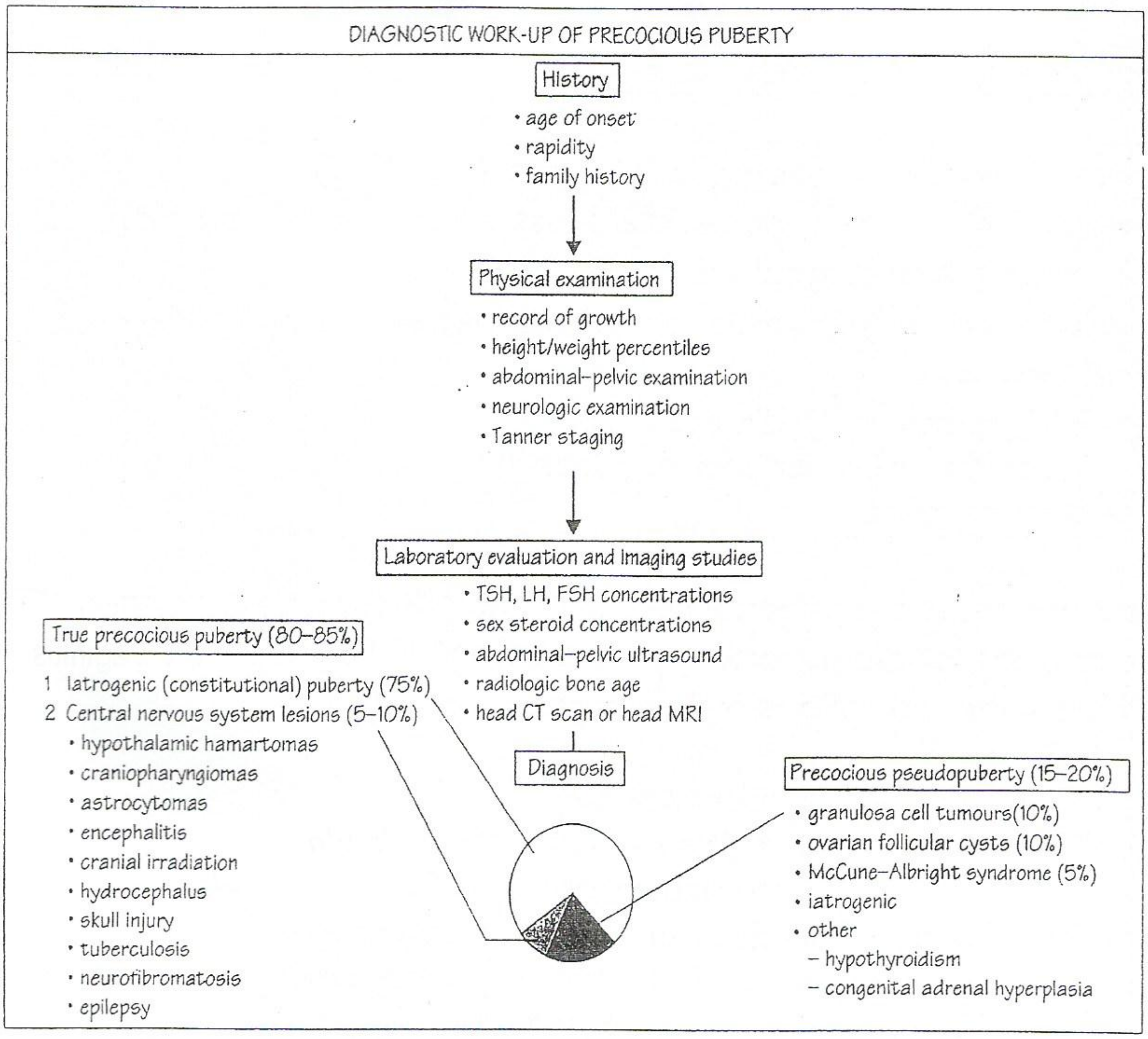
- **Constitutional** ✓, malnutrition, chronic illness
- **Hypergonadotrophic** → ovarian failure
- **Hypogonadotrophic** → hypothalamic – pituitary failure
- **Normogonadotrophic** → end-organ-insensitivity
  (Mullerian agenesis, TFS, imperforate hymen)

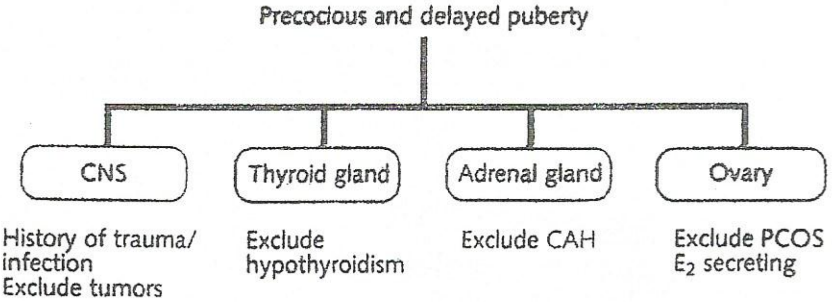
Investigations

LH, FSH to differentiate the 3 types

- *Hyper–gonadotrophic* (FSH > 30 mIU/ mL) → karyotyping
- *Hypo–gonadotrophic* (FSH < 10 mIU/ mL) → CT skull
- *Normo–gonadotrophic* → ultrasound pelvis

Treatment → acc to cause





Note: Chronic illness and some genetic syndromes also cause delayed puberty

History

Fuller Albright (1900–1969), an endocrinologist from Massachusetts, described this monostotic form of fibrous dysplasia of bone with associated patchy skin pigmentation and sexual precocity.

② Precocious puberty

Definition

- Appearance of any pubertal changes earlier than its mean by **2 SD**
- Approximately:- < **8** years for breast & < **10** years for menarche ¤

Etiology

▸ **Isolated (incomplete) = premature:**

1-Thelarche (1 or 2) } no ↑ in E ∴ no ttt
2-Adrenarche } just local tissue sensitivity
3-Pubarche } other pubertal changes occur normally

▸ **Complete**

......Isosexual (↑ E)......		...Heterosexual...
True (central) PP	**False (peripheral) PP**	(↑ An) rare
1-**Idiopathic/ constitutional** ✓ in 90% of cases ¤ early ↘ maturation of HPO axis 2-**Organic brain lesion** trauma / tumors / meningitis ↘ stimulation of HPO axis	1- Est. secreting ovarian tumors 2- Iatrogenic 3- Hypothyroidism 4- McCune Albright $......Triad: ¤ - Precocious Puberty - Polyostotic fibrous dysplasia - Café-au lait patches	1- And sec. tumors: - Ovarian - Adrenal 2- Iatrogenic 3- Cushing 4- Adreno-genital $ (congenital adrenal hyperplasia ✓)
. Normal ovulation Pregnancy can occur	. No ↑ in Gn → no ovulation Only feminization	

Assessment

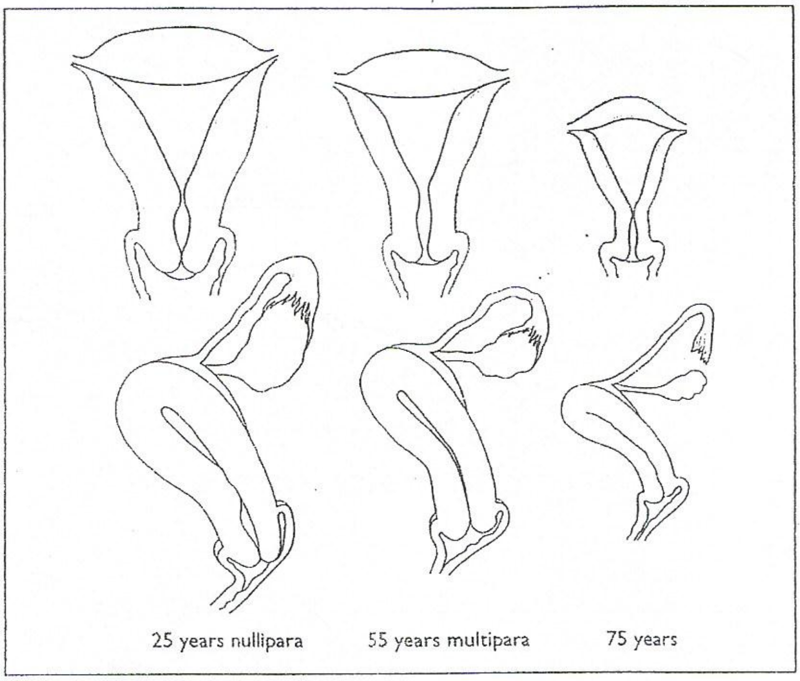
First.....HISTORY & EXAMINATION suggestive of any above disease

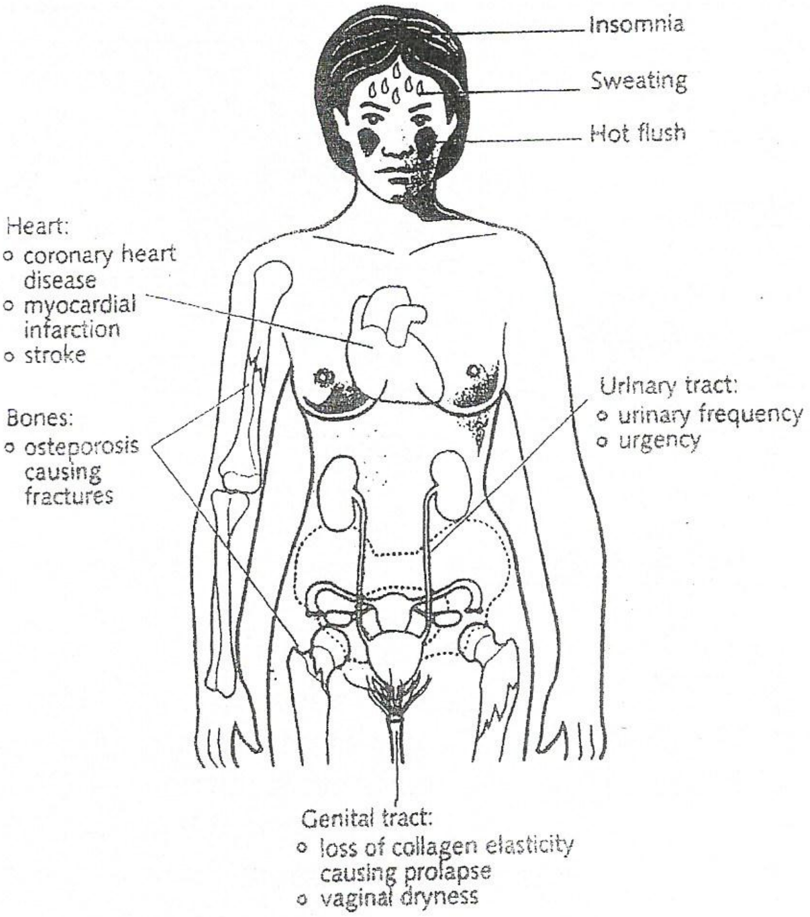
1) Bone age	2) Hormonal assay	3) FSH & LH
▪ Retarded → hypothyroidism ▪ Normal → isolated PP ▪ Advanced → (tall child but...) - Isosexual or - Heterosexual PP	▪ Androgens → heterosexual: - CT abdomen: adrenal tumor - Pelvic U/S: ovarian tumor - 17OH progesterone: CAH ▪ Estrogens → isosexual ⇨ ⇗	▪ High → True → CT brain ▪ Low → False: . Pelvic U/S . T_3,T_4 . Bone scan (McC. Alb)

Treatment

- **Of the cause e.g.** ➡ surgery for ovarian tumor, thyroxin for Juv. hypothyroid.
- **Isosexual** ➡ anti-estrogens ttt till age of 12 yr..................*as in endometriosis*
- **Heterosexual** ➡ anti-androgen.................................*as in hirsutism*

The reduction in the size of the uterus in old age.





The clinical features of menopause.

Menopause & climacteric

❶ HORMONAL changes

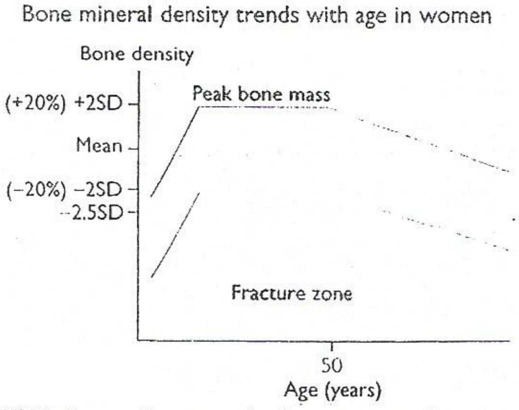
- ↓ E_2 **and inhibin** → d.t. exhausted ovarian follicles
- ↑ **FSH ✓ and LH** → d.t. loss of –ve feedback of $E_{\&}P$
- ↓ **P** → but small amounts are secreted from the adrenal gland ¤
- **T** → continues to be secreted (adrenal -75%- & ovary -25%) by the same levels as before menopause ∴ there is a relative ↑ in **T** ¤
- E_1 → . produced by peripheral conversion from andr. (fat, liver, ms)
  . the main postmenopausal **E** ¤ → weaker than E_2

❷ LOCAL changes

- **Ovaries** → fibrotic, small, no follicles
- **Uterus** → atrophy of all layers (atrophic endomet. is the ✓ cause of PMB)
- **Cx, vulva, vag** → smooth, atrophic, ↓ glycogen → alkaline → infection
- **Supports of genital tract** → weakening → Prolapse or SUI
- **Breast**→ atrophy of glandular tissue + more fat deposition → small & flabby

❸ GENERAL changes

- **Hot flush (flash)**
  - Sudden sense of heat & flushing in face, neck, chest d.t.
    ς attacks of VD → palpitation & sweating then VC → cold shiver
  - Each attack last for few seconds → few minutes
    ς It may be repeated from twice /day → one /15 min
  - Mostly due to *hypothalamic instability* associated with ↑ FSH
- **Cardiovascular**
  - ↑ LDL (*dangerous*) & ↓ HDL (*protective*) → CHD
  - Atherosclerosis (deposition of cholesterol) → hypertension
  - Pdf ⇨ +ve FH, diabetes, obesity
- **Osteoporosis**
  - Progressive systemic bone resorption → ⇩ BMD → ⇧ fractures esp:- («Bone minerals density»)
    ς Cancellous bone: *L.vertebra, femur neck, distal radius*
  - Peak bone mass is acquired at 25 yrs → then rate of bone loss ⇧
    ς From 0.5% /yr up to 2–3 % in post-menop. life
  - Pdf ⇨ +ve FH, cigarette, alcohol, sedentary life, *slim* ¤, *white* ¤
    ⇨ chronic liver /renal, drugs (steroids, heparin, thyroxin)



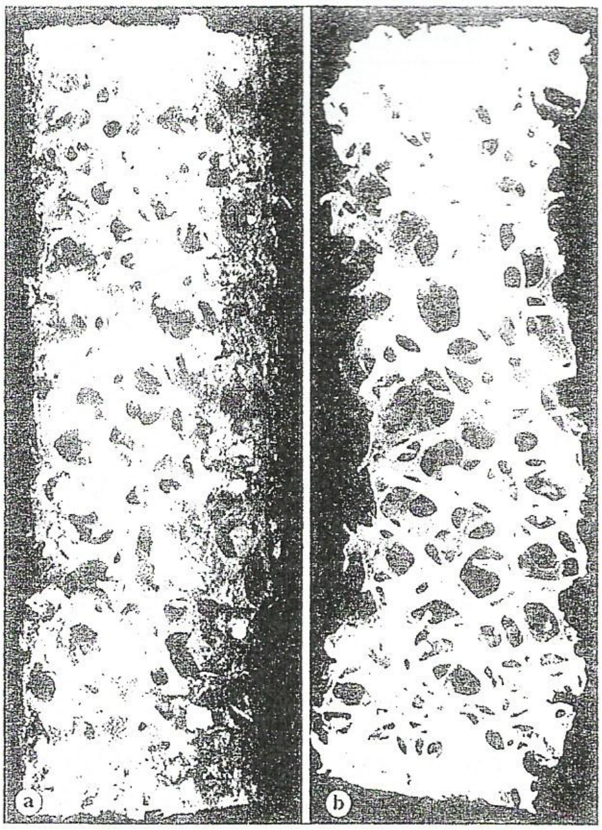
WHO diagnostic categories for osteoporosis

Normal: Bone mineral density not more than 1SD below the mean value for peak bone mass in young adults

Low bone density, or osteopenia: Values between 1SD and 2.5SD below the mean value for peak bone mass in young adults

Osteoporosis: Values more than 2.5SD below the mean value for peak bone mass in young adults

Bone mineral density and osteoporosis.



Osteoporosis: bone from the iliac crest of a 20-year-old woman (a) compared with that of a 60-year-old woman (b).

What is the difference between

- **Osteomalacia** ➨ softening of bones due to defective mineralization (Ca^{++} & P^{+})
  Osteoporosis ➨ ↓ BMD (matrix & minerals < -2.5) → micro-architectural deterioration
  Osteopenia ➨ ↓ BMD with T-score between -1 and -2.5

- **T-score** ➨ comparing BMD with SD of adulTs
  Z-score ➨ comparing BMD with SD of matching gender / age

Definition of Menopause

- The *event* of physiological ***permanent*** cessation of menstruation
  ↘ due to exhaustion of ovarian follicles (**51.4** yr)
- It usually occurs ***gradually***. Rarely it stops suddenly (<10%)
  ↘ with ↓ length of cycles & irregular menstruation
- Menopause is ***diagnosed*** retrograde ¤
  ↘ when menstruation has ceased for 6–12 months in woman > 45 yr

> ☆ CLIMACTERIC ⇨ the *period* during which the female passes from the reproductive to post-menopausal stage (45–52 yrs)
> ☆ PERIMENOPAUSE ⇨ period of life around menopause (before & 1 yr after)
> ☆ POSTMENOPAUSE ⇨ period of life after 1 yr from menopause
> ☆ PREMATURE MENOPAUSE ⇨ ovarian failure < 40 yrs
> ☆ INDUCED MENOPAUSE ⇨ surgical / medical / irradiation

E ⇒ Ductal
P ⇒ alveolar

Menopausal syndrome

the annoying symptoms of ⇩ E (severe in **10%**)

1] **Vasomotor instability** ➡ hot flushes 50–85% ✓
2] **Cardiovascular** ➡ coronary heart disease, hypertension ((CHD & HTN))
3] **Osteoporosis** ➡ rheumatic joint pains, backache, dowager hump
4] **Genitourinary** ➡ .Discharge (senile endometritis & vaginitis), pruritis
.Dyspareunia (dryness of vagina)
.Frequency, urgency, SUI, recurrent cystitis((E→↓↓ glycogen))
5] **GIT symptoms** ➡ dyspepsia, flatulence, change in appetite
6] **Skin** ➡ mild hirsutism (upper lip & chin)
7] **Psychological** ➡ depression, irritability, anxiety, insomnia, ↓ libido

Investigations

- To Confirm
  1. FSH > 25–40 mIU/mL….. most important ✓✓
  2. E_2 < 20 pg/ml……………not important ✗
  3. Vag. cytology…………↓ cornification index (↓ superficial cells) ✗
- For osteoporosis
  1. DEXA ¤ → **D**ual **E**nergy **X**-ray photon **A**bsorptiometry ✓✓
     ↘ Plain X-ray needs loss of > 40% of BMD ✗
  2. Ultrasound → on calcaneous, head of humerus (DEXA is better)
  3. Biochemical markers in urine → urinary collagens ✗
- For CVS → HDL, LDL, triglycerides

RECENT VIEW IN Benefits / Risks of HRT

(Women Health Initiative –WHI study–) 2001 – 2004

	Target	Effect
Definite benefit	. *Vasomotor* . *Genitourinary* *(urethral syndrome)*	↓ 75% in symptoms. However, try to use HRT for flushes for min. time as possible
	Osteoporosis	↑ 5% in bone density, ↓ 30% in fractures. However, try to use other alternative non-hormonal drugs for osteoporosis
Definite risk	- Endometrial cancer ¤	Significant↑ (2-4x). ↓ed by adding 'p'
	- Venous thromboembolism ¤	Significant↑ (2-4x). ↓ed by screening for hereditary deficiency of clotting factors
	- Cardiovascular disease ¤	Significant↑. Therefore no HRT should be used for 1ʳʸ prevention of CHD
Probable ↑ in risk	** *Breast cancer*	Some ↑ related to length of use (esp>5 yr)
	Estrogen protects the normal breast cells from malignant change but it may enhance the growth of some types of *already* existent malignant cells. The other problem is that the highest incidence of breast cancer occurs in old ages (i.e. in the age group who will receive HRT = Bias)	
No proven effect	Quality of life, dementia, cognitive function, sleep, depression, sexuality	

Hormone Replacement Therapy

Indications

1. *Symptoms* of estrogen deficiency (menopausal syndrome)
2. *Asymptomatic* women with high risk for *osteoporosis* or *CHD*
3. *Routine* for all postmenopausal women
4. Premature ovarian failure (POF)

Contraindications

Absolute ¤	Relative
Unexplained vag. bleeding: cr ??	Endometriosis (⇑ Estrogen)
Active liver disease	- Chronic impaired liver function - Gall bladder disease
- Recent myocardial infarction - Recent / active vascular disease	-Controlled hypertension ¤ & DM ¤ aren't contraindication
History of estrogen related DVT	Thrombophlebitis

Mechanism of action

- **Protection from osteoporosis by**
  - ⇓ action of osteoclasts (through inhibiting effect of parathormone)
  - ⇑ Ca^{++} (↑ GIT absorption, ↓ renal loss, stimulation of calcitonin)
- **Protection from CVD by**
  - ⇑ HDL, ⇓(LDL & cholesterol) } recently masked by
  - ⇓ cholesterol deposition in vessels ± VD } the ↑ in CV accidents

Work up needed before HRT

* *History taking*
* *Physical examination* (Blood Pr., weight, breast, PV)
* *Investigations*:
  - General ⇨ FBS, lipid profile (± liver function tests)
  - Local ⇨ mammogram✓, Pipelle & Pap smear (if bleeding)

Duration of therapy

- Start at any age after menopause (never too late)
- Some say 10 years are the minimal
- Others → HRT must be given for life
- The most recent (& correct) → not recommended for > 2 yrs ✓✓✓

❶ ESTROGENS ONLY (ERT)

▸ **ORAL THERAPY**
- *Indicated only* → if the uterus is removed (∴ no need for 'P')
- *Drugs* . CEE (Premarin): 0.625–1.25 mg /d
  . Estriol (Ovestin) 1 mg /day

▸ **NON-ORAL**
- *Drugs*
  1] **Skin patch** (estraderm) → applied twice weekly (0.05 mg)
  2] **Skin gel** (estragel) → applied twice daily to arms or legs
  3] **Vaginal Cream** (premarin) → for atrophic vaginitis & dyspareunia
  4] **Subcutaneous Implant** 1mg → inserted in abdominal wall / 6 m
- *Indications* ....they by-pass GIT & liver...............
  1. Malabsorption syndrome
  2. They give a higher E_2 concentration, ∴ given in:
     . Failure of oral therapy to control symptoms
     . Severe cases e.g.: osteoporosis
  3. Metabolic disorders e.g. DM, HTN
  4. History of DVT: oral estrogen stimulates the liver to ↑ clotting factors & ↓ anti-thrombin III

❷ COMBINED E & P THERAPY (HRT)

▸ A progestogen must be added if the uterus is present to prevent.......
▸ It may be given *alone* to relieve hot flushes
▸ *Regimens*
1. Cyclic (sequential)
   - CEE 0.625 mg/day + MPA 10 mg /d for 10–14 days
   - But leads to cyclic withdrawal bleeding
2. Continuous ✓✓
   - CEE 0.625 mg + MPA 2.5 mg daily
   - It avoids withdrawal bleeding

Recently, the WHI study proved that ERT leads to

Definite ⇧ in risk of endometrial cr ¤, venous thromboembolism ¤, CVD ¤
Probable ⇧ in risk of breast cancer (related to length of use)
No proven effect on quality of life, dementia, depression, sleep, libido
Non-hormonal drugs are better used for menopausal symptoms

③ Non-hormonal Drugs

▸ **SERM** ✓

- Selective Estrogen Receptor Modulators (agonist antagonist) are drugs which stimulate different estrogen receptors (α,β).. ∴
  - . Exert estrogenic effects on desired tissues (CVS & bones)
  - . Avoids estrogen stimulation on others (uterus, breast)
- Commonest drugs are ***Tamoxifen*** (1st generation).... ***Raloxifen***

▸ **Tibolone** (Livial) ✓

- Synthetic steroid with **weak** *est*, *progest*, *androg* effect
- Good relieve of menopausal symptoms, also:
  - . ***Estrogen*** doesn't stimulate uterus or breasts
  - . ***Progesterone*** has no need to be added
  - . ***Androgen*** improves osteoporosis & LIBIDO
- Dose → 2.5 mg tablet /day

▸ **For hot flushes**

- *Agreal, bromocriptine* (dopamine agonists)
- *Clonidine patch* (twice weekly), α methyl-dopa
- *Phyto-estrogens* ✓ (natural 'E' found in soya beans)

▸ **For osteoporosis**

Prophylaxis ✓✓✓

- . Cessation of smoking & alcohol
- . Regular weight bearing exercises
- . Adequate intake of Ca & vit D form adulthood
  - **Calcium** → 1000 mg daily } slows bone loss but don't
  - **Vitamin D** → 800 IU daily } ↑ the bone mass

Estrogen ✗

- . CEE 0.625 mg daily (or SC E_2 implants 1mg)
- . Given mainly for the 1st 10 yrs (max rate of bone loss)
- . If HRT is stopped → rebound bone loss ∴ better to give ↓

Non-hormonal therapy

- ***Bisphosphonates*** ✓ (→ expensive) inhibit OSTEO-CLASTS ⇨ ↓ bone resorption
  - . They are the most potent ¤ → ↑ BMD by 10% after 1 year
  - . Alendronate (Fosamax) → 10 mg /day or 70 mg once wkly
- ***Clacitonin*** (salmon) ⇨ intranasal spray 200 IU (miacalcic)
- ***Fluoride*** ⇨ the only known OSTEO-BLASTIC drug ¤
- ***Teriparatide*** I.M. for 2 yrs ⇨ anabolic bone effect – *recent* –

Causes of amenorrhoea

Reproductive outflow tract disorders

- Asherman's syndrome
- Müllerian agenesis
- Transverse vaginal septum
- Imperforate hymen
- Testicular feminization syndrome

Ovarian disorders

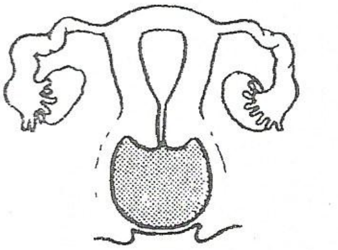
- Anovulation, e.g. polycystic ovarian syndrome (PCOS)
- Gonadal dysgenesis, e.g. Turner's syndrome
- Premature ovarian failure
- Resistant ovary syndrome

Pituitary disorders

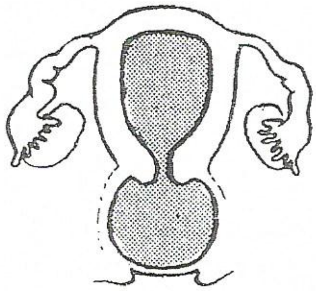
- Adenomas such as prolactinoma
- Pituitary necrosis, e.g. Sheehan's syndrome

Hypothalamic malfunctions

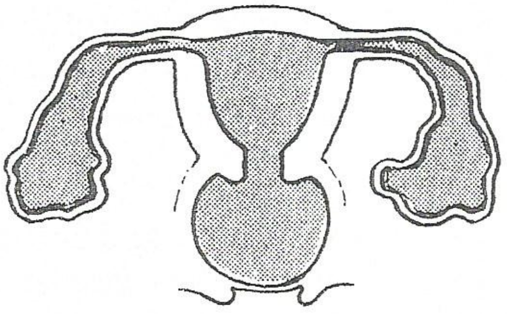
- Resulting from excessive exercise
- Resulting from weight loss/anorexia nervosa
- Resulting from stress
- Craniopharyngioma
- Kallman's syndrome



Haematocolpos Only the vagina is distended by altered blood.



Haematometra The uterus is also distended.



Haematosalpinx In longstanding cases the tubes are also involved.

imperforate hymen

✳ Amenorrhea ✳ absence of menses

Types

- 1ry amenorrhea

  Absence of menstruation in a patient who has <u>never menstruated before</u>, either at: **14 years** → without 2ry sexual characters,
  16 years → with 2ry sexual characters

- 2ry amenorrhea

  Cessation of menstruation for a period equal to
  3 cycles → if previous menses were regular, or
  6 months → if they were irregular or infrequent

Etiology

Physiological

- **Before puberty** ➡ Gonadotrophin secretion not yet established
- **After menopause** ➡ despite ↑↑ GnRH (d.t. exhaustion of follicles)
- **During pregnancy**✓ ✓ ➡ continuous placental steroid production (E+P)
- **During lactation** ➡ *Prolactin* (1- ↓ GnRH, 2- ↓ Gn action on ovary, 3- ↓ovarian steroidogenesis, 4- ↓ action of E)

Pathological

↓

❶ False amenorrhea (Cryptomenorrhea)

▶ **Etiology (outflow tract obstruction)**
- Imperforate hymen ✓ (the commonest cause ¤)
- Transverse vaginal septum / vaginal aplasia
- Congenital cervical atresia

▶ **Symptoms ¤ (starting at puberty)**
- 1ry amenorrhea → cryptomenorrhea (false amenorrhea)
- Cyclic lower abdominal pain
- Abdominal swelling (mainly hematocolpos ¤)
- Pressure manifestations: as dysuria & retention of urine ✓

▶ **Signs**
- Abd. ⇨ tense cystic pelviabdominal swelling
- Vag. ⇨ bluish bulging hymen
- P/R✓⇨ distended vagina (continuous with the abd. swelling)

▶ **Complications**

Haematocolpos, haematometra, haematosalpinx → spillage of blood into peritoneal cavity → adhesions → infertility (∴ don't postpone!)

▶ **Treatment**
- General anesthesia + catheterization
- Cruciate incision ⊗ + excision of edges OR
  .Opening a hole in the hymen after traction from its center
- Leave blood to drain slowly + antibiotics coverage

Hypothalamus -IV-

1- <u>Congenital syndromes</u>

- **Frohlich** → * ↓ GH RH → ↓ height, central obesity
  * No GnRH → amenorrhea, genital hypoplasia, no 2ry sexual ccc
- **<u>L</u>aurence <u>M</u>oon <u>B</u>iedl** → - <u>L</u>imb deformity......Polydactly / Syndactly
  As Frohlich + - <u>M</u>ental......................Retardation
  - <u>B</u>lindness.................Retinitis pigmentosa ¤
- **Kallmann syndrome** → * Amenorrhea (isolated GnRH deficiency)
  * Anosmia (d.t. common embryological pathway ¤)

2- <u>Traumatic</u> ➟ fracture base of the skull

3- <u>Inflammatory</u> ➟ after meningitis or encephalitis

4- <u>Tumors</u> ➟ destroying the hypothalamus

5- <u>Miscellaneous</u>

- **Hyperprolactinemia of hypothalamic origin**
  ς due to loss of -ve feedback of PIF (dopamine) by drugs / lesions
- **Postpill amenorrhea** (Shearman syndrome)
  ς persistence of hypothalamic suppression after stopping COC
  ς If am. lasts > 6 months → search for causes other than pills
- **Psychological conditions**

  a- <u>Severe stress</u> (extreme grief – war), **severe exercise or rapid weight loss** (Ballet dancers – Joggers) → ↑ prolactin & β-endorphins
  → ↓ pulsatile GnRH secretion

  b- <u>Anorexia nervosa</u> → severe psychological disturbance affecting both: hypothalamus & appetite → marked anorexia, emaciation, hypoglycemia, low BMR

  c- <u>Bulimia</u> → characterized by binge purge eating (episodes of overeating) followed by → self induced vomiting, fasting, use of laxatives & diuretics

  d- <u>Pseudocyesis</u> → extreme desire to get pregnant (infertile patients) or marked fear from it (near menopause) ⤸
  - amenorrhea (d.t. ↓ GnRH secretion)
  - abdominal distension (fat, gas, increased lordosis)
  - fetal kicks (intestinal movement)

Pituitary -III-

1- Congenital

* **Levi-Lorain syndrome:**

= ↓ GH + ↓ gonadotrophins → dwarfism + amenorrhea

2- Post-traumatic

3- Post-inflammatory

4- Pituitary tumors

> Cushing syndrome (↑ed suprarenal cortical activity)
> C/P: ↑ cortisol → amenorrhea, trunkal obesity, moon face, striae, Hypertension, hyperglycemia, osteoporosis
> ↑ androgen → acne, hirsutism
> Etiology
> - Pituitary (C.disease) → basophil adenoma
> - Adrenal (C.syndrome) → adenoma / adenocarcinoma
> - Hypothalamic → ↑ ACTH production
> - Ectopic ACTH production → e.g. oat carcinoma of lung
> - Congenital adrenal hyperplasia ✓

* **Destructive** → e.g. craniopharyngioma

* **Secretory:**

- PROLACTINOMA (usually chromophobe adenoma) ➡ prolactin
- Acidophil adenoma ➡ GH → acromegaly or gigantism
- Basophil adenoma ➡ ↑ ACTH → bilat. ad. Hyperplasia

5- Miscellaneous

☆ *Empty Sella syndrome*

1^{ry} → congenital herniation of subarachnoid space into the sella turcica

2^{ry} → exposure of pituitary to surgery, infarction, tumors, irradiation

. Effect (↑ CSF) → Gradual enlargement of the sella turcica

↳ Compression of pit. gland → amenorrhea

↳ Compression of pit. stalk → hyperprolactinemia

. Diagnosis → CT, MRI

☆ *Simmond's disease* Pan-hypopituitarism (pit. cachexia) d.t. any cause

☆ *Sheehan's disease*

▸ Etiology

Panhypopituitarism due to necrosis of *anterior* pit after severe APhge or PPhge as

- The anterior lobe enlarges in preg. > its vascular supply
- Shift of blood to post. lobe in labor to secrete oxytocin

▸ C/P

↓ **FSH & LH** → amenorrhea + infertility + genital atrophy

↓ **TSH** → 2^{ry} hypothyroid. → weakness, cold intolerance, constipation

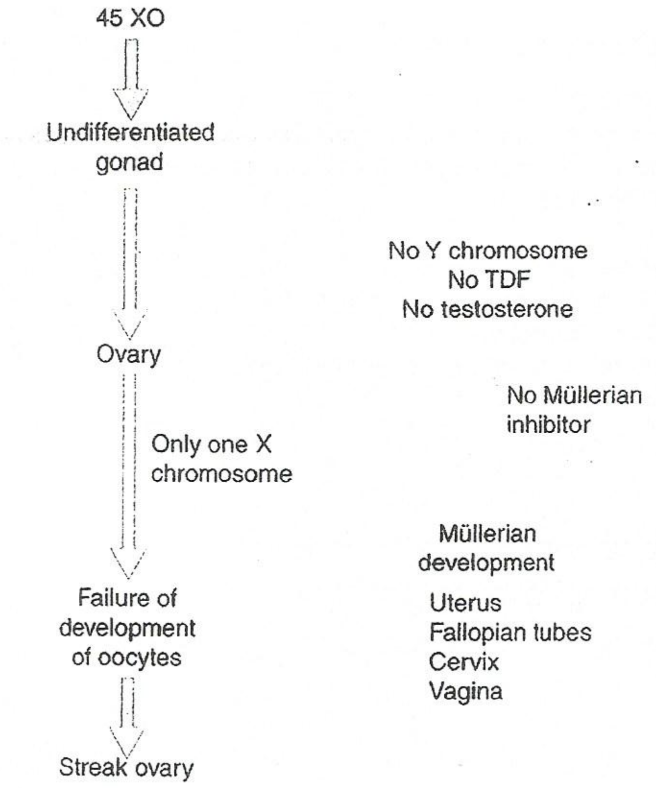
↓ **ACTH** → adrenal insufficiency

↓ **GH**

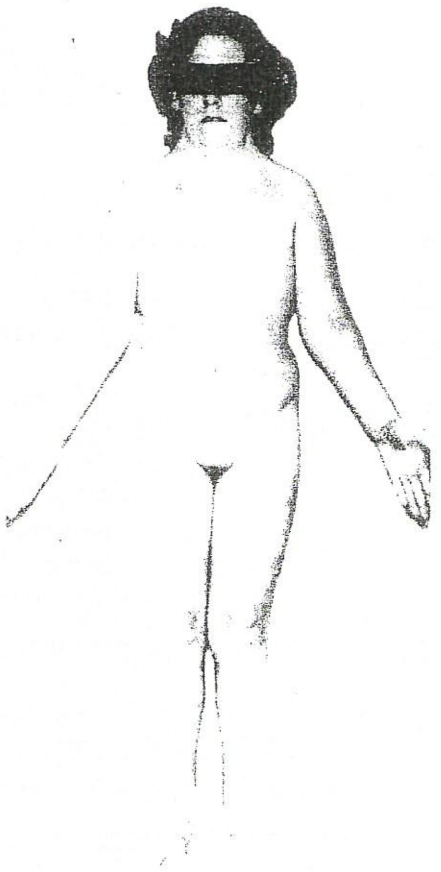
↓ **prolactin** → failure of lactation (1^{st} manifestation in Sheehan)

↓ **MSH** → decreased pigmentation

▸ Treatment: replacement therapy of the deficient hormones



Turner's syndrome. (TDF, testicular determining factor.)



Turner's syndrome.

History

Henry Hubert Turner (1892–1970), an endocrinologist from Illinois, described a syndrome in 1938 characterized by sexual infantilism, short stature and webbing of the neck. The same condition was described in Europe as Bonnieve–Ullrich syndrome by Otto Ullrich in 1930.

History

Kallmann's syndrome was described in 1944 by Franz Josef Kallmann, a German-American geneticist, although others – such as the Spanish physician Aureliano Maestre de San Juan (1828–1890) – had noticed a correlation between anosmia and hypogonadism in 1856.

Ovary -II-

1- **Congenital**
- Agenesis / Dysgenesis (pure, mixed, Turner✓✓, others)
- Testicular feminization syndrome
- Superfemale (47xxx)

2- **Traumatic** → oophrectomy (surgical, medical, irradiation)

3- **Inflammatory** → mumps, T.B.

4- **Neoplastic**
- Destructive tumors → bilateral
- Secretory
  . ⇧ E ➡ estrogen producing tumors
  . ⇧ An ➡ androgen secreting tumor
  . Both ➡ Polycystic ovarian disease ✓

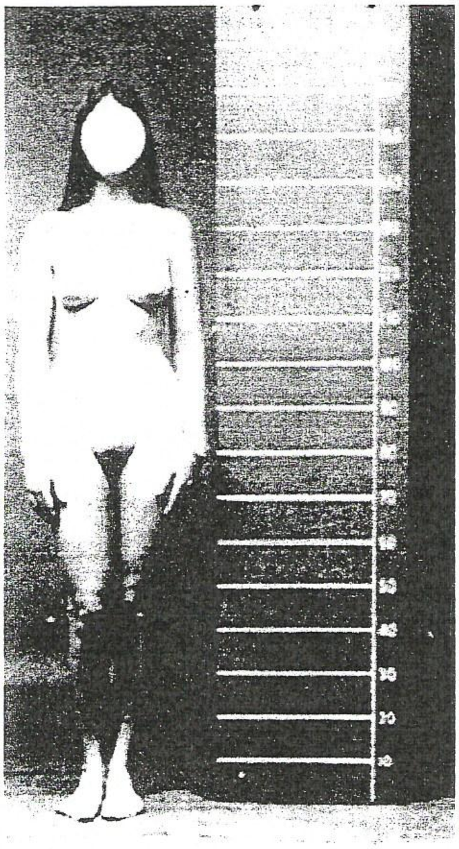
5- **Miscellaneous**
- Premature ovarian failure
- Resistant ovary syndrome
- Hyperprolactinemia
- Hyperandrogenism

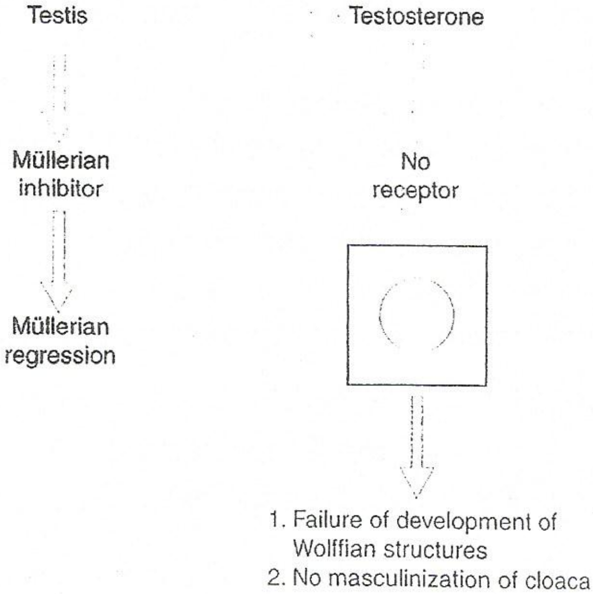
♣ Turner syndrome

- **Clinical picture**
  - Genotype → 45 chromosomes (45xo) i.e. no Barr body ¤
    OR ↘ Mosaic (45xo – 46xx) or Chimerism (45xo – 46xy)
    ↘ may be tall / get menses – pregnant / but finally….POF
  - Phenotype
    . Short < 150 cm, webbed neck
    . Shield chest (widely spaced nipples + underdeveloped breasts)
    . Coarctation of aorta ¤ , cardiac & renal abnormalities
    . Cubitus vulgus (wide carrying angle)
  - External genitalia → infantile
  - Internal genitalia → streak ovaries (fibrous bands + no follicles)
- **Suspected in neonate by** ¤ → lymphedema of dorsum of hands & feet
  → Short 4th metacarpal
- **Investigations:** ↓ E + ↑ FSH (hypergonadotrophic hypogonadism)
- **Treatment**
  1- Cyclic E&P
  - To stimulate breasts, menstruation, prevents osteoporosis & CVD
  - Not given < 13 yrs (bone age) to avoid premature closure of epiphysis
  - Growth hormone can be added to increase height (± 8cm)

  2- Oophrectomy is done only in mosaic types with Y-chromosome
  ς risk of malignancy is → 25%: dysgerminoma

  3- The only hope in pregnancy → oocyte donation ✗





XY female – androgen insensitivity.

♣ Testicular feminization (Androgen Insensitivity Syndrome)

- **Pathogenesis**

  X-linked recessive diseases → *absent* or *insensitive* receptors in breasts, hair follicle, vulva → no response to ANDROGENS secreted from testis (i.e. end organ insensitivity) → ∴ they develop in a feminine direction

- **Clinical picture**
  - Karyotype ⇨ 46 XY (male)¤
  - Phenotype
    - * Complete form ➡ attractive female with well developed breasts (fat only – no glands) with small nipples, pale areola, pubic & axillary hair are absent
    - * Incomplete form ➡ variable degree of masculinized female
  - Internal genitalia ⇨ testis (found intra-abdominally, in a hernial sac, in groin, in labia). They secrete a hormone from sertoli cells (anti-Mullerian hormone) → no uterus, tubes
  - External genitalia ⇨ a vaginal pouch ¤

- **Investigations**
  - Normal ♂ level testosterone (> 300 ng/dl)
  - Normal ♂ level estradiol (30 pg/ml) produced from
    - . Adrenals, testis, peripheral conversion (androstenedione to estrone)
    - . This small E amount is unopposed by T → breast development
  - Normal FSH, LH levels

- **Treatment**
  1- Leave the patient till 16-18 years: to allow breast development
  ↳ followed by gonadectomy (a must as → malignancy is 25%)
  ↳ followed by ERT (no need for progesterone):
  To maintain the feminine character, avoid osteoporosis, CVD
  2- For vaginal pouch → gradual dilatation or plastic surgery

---

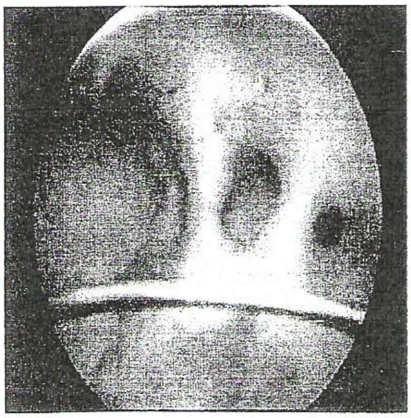
♣ Superfemale (Triple X syndrome)

- Genotype → 47xxx OR 48xxxx
- Phenotype → majority are normal (may have lowered IQ)
- External genitalia → infantile, amenorrhea, infertility
- Treatment → induction of ovulation

♣ Others

- Partial deletion of short arm (46xx p-)
- Deletion of long arm (46xx q-)
- Isochromosome of x chromosome

Ashermann syndrome diagnosed by HSG



Ashermann syndrome seen by hysteroscope

◈ Uterus -I- ◈

1- **Congenital** → aplasia, hypoplasia
2- **Inflammatory**
3- **Traumatic** → Hysterectomy or ↓

Asherman syndrome ✍

(amenorrhea traumatica, intrauterine synechiae)

- *Etiology*: Φ
  - Ut. operations ➡ excess D&C–basal layer–, myomectomy, metroplasty manual removal of placenta, intra-cavitary radiation
  - Ut. infections ➡ septic abortion, puerperal sepsis, T.B. endometritis

- *Types*

  Evaluated by Hysteroscopy

	Uterine adhesions	Tubal ostia
Minimal	< ¼ involved	both are seen
Moderate	¼ – ¾ involved	one is seen
Severe	> ¾ involved	none is seen

- *C/P* ➡ 1. Amenorrhea, hypomenorrhea
  2. Infertility
  3. If got pregnant → . Habitual abortion / Preterm labor
     . Placenta previa / Placenta accreta

- *Diagnosis*
  - *History:* of any of the etiologic factors
  - *Examination:* limited mobility of the uterine sound
  - *Investigation*: .–ve E+P challenge tests with normal FSH & LH levels
    . adhesions are seen by HSG, hysteroscope (best)

- *Treatment*
  - **Adhesiolyis** ➡ D&C (or better hysteroscopic) ± antibiotics
  - **Avoid new adhesions by** ➡ Foley's catheter for 10 days
  - **Induce new endometrium** ➡ cyclic E+P in high doses (CEE 2.5mg daily)

◈ General ◈

- **Endocrine** - Thyroid (hypo or hyper)
  - Adrenal (hypo or hyper)
  - Acromegaly
- **General debilitating disease** - Severe anemia & malnutrition
  - Chronic diseases as T.B. / D.M. / R.F.
- **Drugs** - Drugs causing hyperprolactinemia ♒
  - Drugs containing hormones: . anabolic steroids, androgens / danazol
    . continuous COC / progestins / GnRH

Summary of clinical management

Initial management:

- Exclude pregnancy.
- Ask about perimenopausal symptoms (e.g. flushings, vaginal dryness).
- Take a history including weight changes, drugs, medical disorders and thyroid symptoms.
- Carry out an examination, looking particularly at height, weight, visual fields and the presence of hirsutism or virilization. Also carry out a pelvic examination, unless this is contraindicated.
- Check serum for LH, FSH, prolactin, testosterone, thyroxine and thyroid-stimulating hormone (TSH).
- Arrange a transvaginal ultrasound scan, looking for polycystic ovaries.
- Review with the results .

- 1^ry^ amenorrhea ➡ FALSE (cryptomenorrhea) → cyclic pain
  TRUE → most common causes are (CONSTITUTIONAL✓):
  1. **Ovarian dysgenesis (30%)**
  2. **Mullerian agenesis**
  3. **Testicular Feminization Syndrome**
- 2^ry^ amenorrhea ➡ 1^st^ thing exclude pregnancy (the commonest)
  1. **PCO**
  2. **Hyperprolactinemia**
  3. **hyperandrogenism**
- Hypomenorrhea ⇨ ↓ amount/ duration of menstruation
- Oligomenorrhea ⇨ infrequent menstruation (>35days)

Both hypo/oligo may be constitutional or endocrine in origin. Should be investigated & treated same as in amenorrhea; but prognosis is better

ℑ Assessment ℑ

➊ History ↘

Personal

- Age----------------to differentiate 1^ry or 2^ry or physiological (<9 or >40)
- Marital status-----to exclude pregnancy
- Parity--------------previous pregnancy
- Occupation-------stress / ballet dancers

Complaint----------------amenorrhea

History of present illness: Amenorrhea +

▸ **Other Gynecological problems:**

- *Estrogen (anovulation)* . Short amenorrhea followed by PPI bleeding
  . Infertility
  . Secondary sexual ccc (breast / hair)
- *Virilization* → hirsutism, acne (e.g. PCO)
- *Galactorrhea*

▸ **Other Endocrinological problems:**

- HYPOTHYROIDISM ⇔ cold intolerance, easy fatigability, constipation
- CUSHING ⇔ obesity, striae, fatigue, hirsutism, muscle weakness
- ACROMEGALY ⇔ enlargement of hands, feet & facial structure
- DIABETES ⇔ polyuria, polydypsia, polyphagia, pruritis

▸ **Other system problems:**

- Severe anemia → pallor, palpitation, easy fatigability
- T.B. → chest troubles

Menstrual history

- Menarche ----
- Cycles--------- were regular or not
- Cyclic symptoms------suggestive of cryptomenorrhea

Obstetric history ⊃ POSTPARTUM AMENORRHEA ⊋

- Lactational
- Another pregnancy
- Uterus → Ashermann or hysterectomy was done
- Pituitary → Sheehan syndrome

Past history

- Medical ---- TB, DM, endocrine
- Surgery ---- hysterectomy, $D_{\&}C$, ovarian surgery
- Drugs ------ drugs causing hyperprolactinemia

Contraceptive history

- Postpill amenorrhea
- Amenorrhea following injectable contraceptives

❷ Examination ↘

☆ Primary amenorrhea

- **General** ⟹
  - .Phenotypic character….*Turner* stigmata
  - .Pubertal development….*Tanner* staging
- **Local** ⟹
  - .Hymen inspection…..cryptomenorrhea
  - .Clitromegaly………..ambiguous genitalia
  - .PR (in virgins)……...absent uterus

☆ Secondary amenorrhea

First of all…exclude pregnancy

▲ **Height** - SHORT → Frohlich / LMB / Levi-Lorain / Turner
- TALL → gigantism / acromegaly / TFS

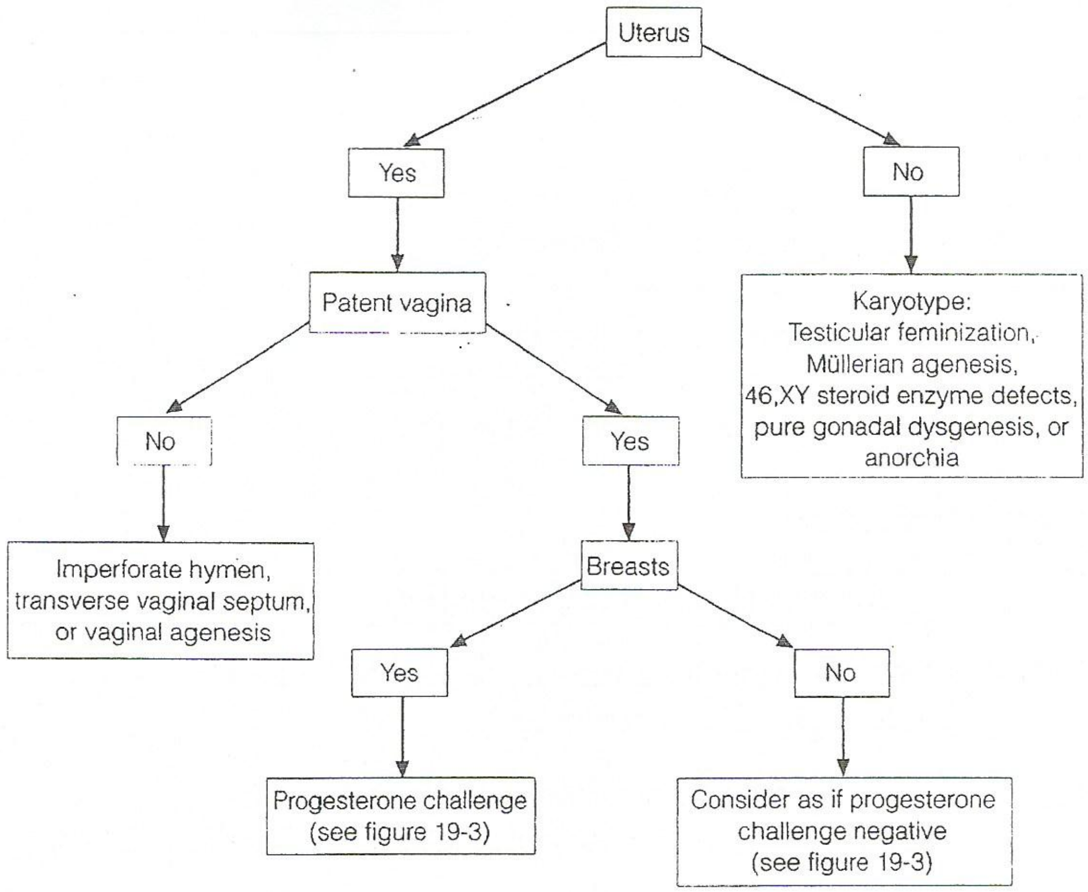
▲ **Weight** . THIN → anorexia nervosa / hyperthyroid / DM
. OBESE → PCO / hypothyroid / Cushing / Frohlich / LMB

▼ **Amenorrhea** + **galactorrhea** → causes of hyperprolactinemia
▼ **Amenorrhea** + **virilization** → PCO, CAH, androgen sec. tumor

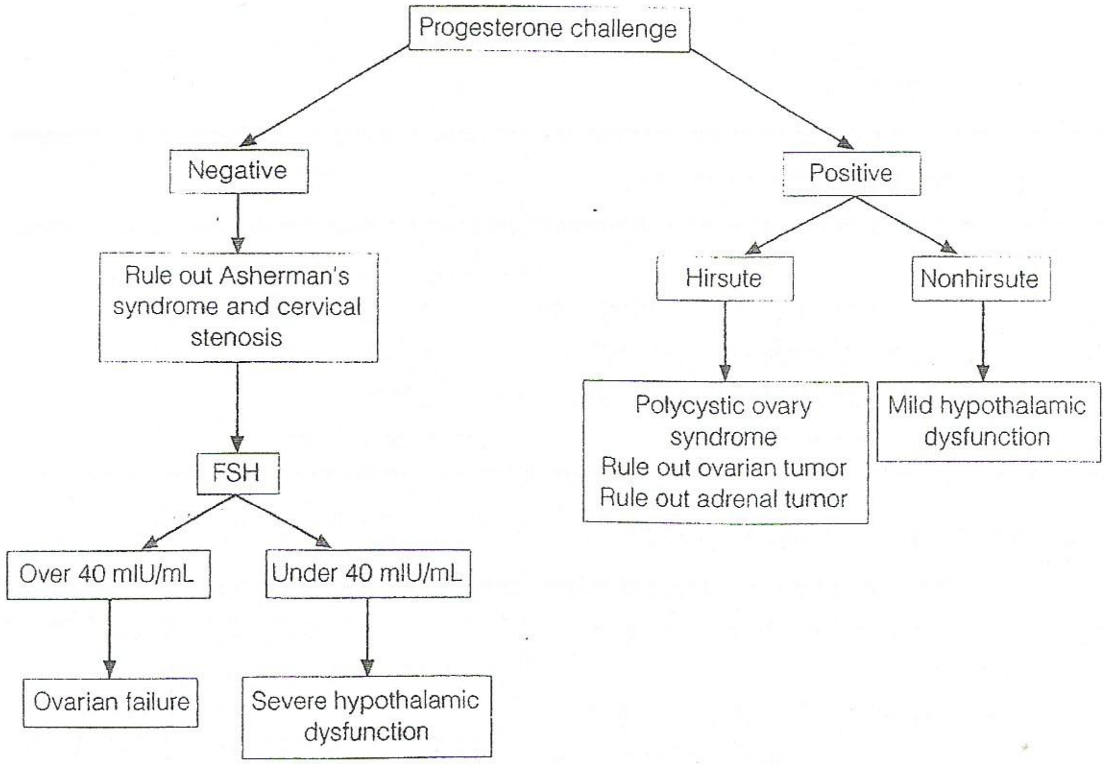
▶ 2^{ry} **sexual characters**

Uterus present (absent breast) ¤	**Both present**
.**Gonadal failure** ç hypergonadotrophic hypogonadism .**Pituitary & hypothalamic** –SYNDROMES- ç hypogonadotropic hypogonadism .**General constitutional cause**	. Acquired causes (2^{ry} amenorrhea) - HPO- axis - Uterus .Cryptomenorrhea

Breast present (absent uterus) ¤	**Both absent (1%)**
. **Testicular feminization syndrome** . **Mullerian agenesis** - differentiated by .Testosterone level .Absence of hair . **Congenital** Asherman syndrome	Enzymatic pathway defects in testosterone synthesis in xy **Cong. lipoid adrenal hyperplasia** **17α-hydroxylase deficiency** **17-20 desmolase deficiency**



• Diagnostic flowchart for patients with primary amenorrhea.



• Diagnostic flowchart for patients with secondary amenorrhea.

③ Investigations ↘

◈ **First of all** → exclude **pregnancy** → β-HCG ¤¤

◈ **Then determine level** . **Prolactin** level.........
. **TSH** ± T_3, T_4.........

➡ **Progesterone challenge test:** 5mg 1x2x10 or DMPA (150 mg IM)
+ve bleeding → means that the ovary is producing estrogen but there is no progesterone i.e. no CL i.e. anovulation
–ve bleeding → either:
- Ovary doesn't produce estrogen e.g. Turner
- Uterus is not responding e.g. synechiae, hypoplasia

➡ **E + P withdrawal test:** COC for 3 weeks
–ve bleeding → i.e. problem in uterus i.e. refractory endometrium
ç uterine investigations → sound,.......,.....,.......,...
+ve bleeding → i.e. No estrogen i.e. problem is in the HPO axis

➡ **Serum FSH, LH**
High FSH (> 40 mIU/mL) → ovarian failure
Low FSH (< 5 mIU/mL) → either: Hypothalamus / Pituitary

➡ **GnRH test + CT / MRI**
FSH increased → hypothalamic problem
FSH not increased → pituitary problem

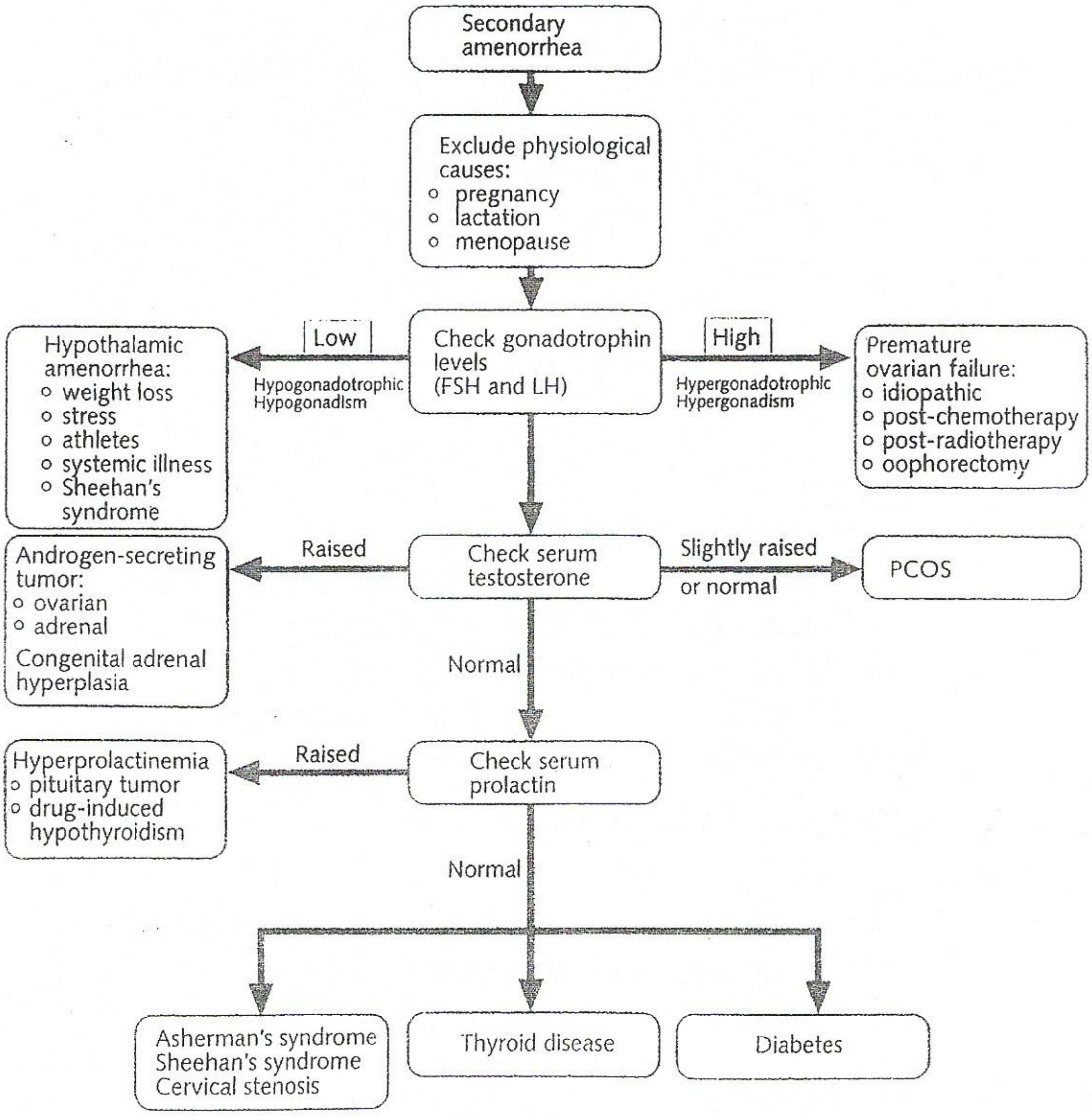
◈ **Others:**

▸ *Hyperandrogenism*
- Adrenal gland investigations:
  . DHEA-S → diagnose adrenal origin
  . Cortisol & ACTH level → in Cushing
  . 17-OH progesterone → in CAH
  . CT / MRI → to exclude tumors
- Testosterone level (diagnose ovarian origin)

▸ *Hyperprolactinemia*.....Prolactin level ±CT brain

▸ *1ʳʸ amenorrhea*
- Turner syndrome → karyotyping ± laparoscopic ov. biopsy
- Mullerian agenesis → U/S (absent uterus)
- Test. Feminization → testosterone level

Role of U/S in amenorrhea
* **Uterus**...absent (Mullerian agenesis /TFS)...infantile (uterine index <1)
...absent normal trilaminar endomet is suggestive of Ascherman
* **Ovaries**........absent (Turner).....swelling (PCO /functional cyst /neoplasm)
* **Vagina**........hematocolpos & hematometra



Algorithm for secondary amenorrhea.

Management

General

- Correct anemia & malnutrition
- Reduction of weight if obese
- Alleviate stress

Primary amenorrhea

- **Normo-gonadotrophic**
  - Imperforate hymen..........cruciate incision
  - Mullerian agenesis...........neo-vagina (vaginoplasty)
  - Testicular feminization.......gonadectomy at 18 yrs
- **Hypo-gonadotrophic**
  - Hypoth-pituitary causes......cyclic HRT or HMG/HCG
- **Hyper-gonadotrophic**
  - Ovarian (Turner).............cyclic HRT at 13 yrs

Secondary amenorrhea

- **Hormonal**
  - *Cyclic HRT ⇨ POF*
    Cycloprogynova (estradiol valerate + norgestrel)
    Yasmin / Gynera
    Cyclic progestogen for 7–10 days /month
  - *Induction of ovulation ⇨ PCO*
    Clomiphene citrate (clomid)
    HMG / HCG
  - *Hyperprolactinemia*
    Dopamine agonists (parlodel – dopergine – dostinex)
  - *Hyperandrogenism*
    Androcur (cyproterone acetate) / Spironolactone / Diane
  - *Thyroid dysfunction*
    Eltroxin in hypothyroidism
    Thiouracil in thyrotoxicosis
- **Surgical**
  - PCO.........................laparoscopic ovarian drilling
  - Asherman syndrome.........hysteroscopic resection
  - Pituitary adenoma only if....refractory to medical ttt
  - Resection of..................adrenal tumor

✳ Anovulation ✳

Definition

Failure of ovulation, which may be classified into ⤸

Group I	Hypothalamic pituitary failure	Low......LH & FSH
Group II	Hypothalamic pituitary dysfunction	Normal...LH & FSH
Group III	Ovarian failure	High......LH & FSH

Etiology

- **Physiological** ➡ prepubertal, postmenopausal, pregnancy & lactation
- **Pathological** ➡ Hypothalamus.../pituitary.../thyroid.../adrenal.../ovary...
- **General** ➡ severe malnutrition, anemia, DM, TB, exercise, stress
- **Idiopathic** ➡ most frequent (functional error in the HPO axis ?) ✓✓
- **Iatrogenic** ➡ COC, androgens, drugs inducing hyperprolactinemia

Clinical picture

➡ **C/P of anovulation**

1. Menstrual irregularity → amenorrhea, oligo-hypomenorrhea, DUB
2. Infertility

➡ **C/P of etiology** (as in amenorrhea) ♒**.......e.g:**

1. PCO → SOHA
2. Hyperprolactinemia → galactorrhea
3. Hyperandrogenism → hirsutism
4. Other endocrine disease → thyroid (goiter, tremors)

Investigations

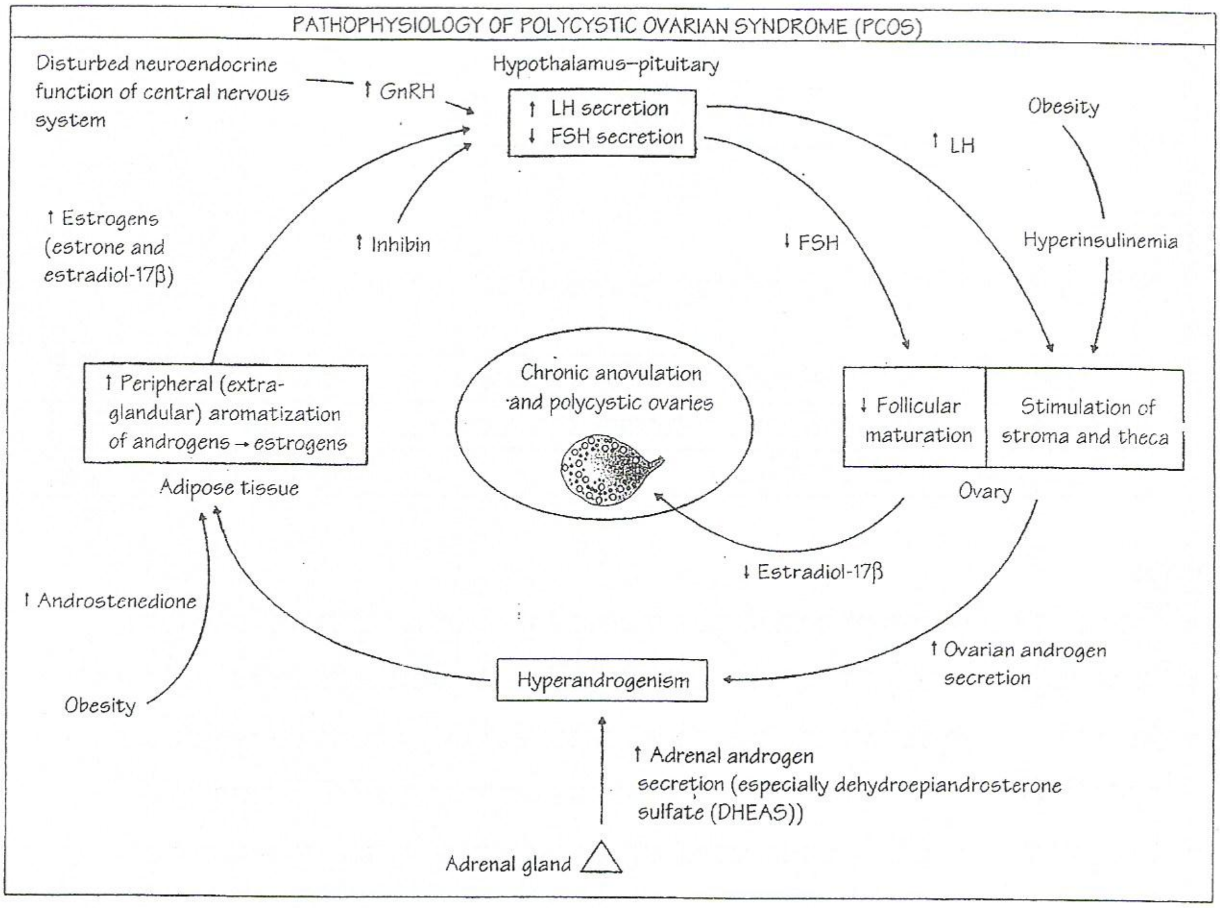
➡ **Tests for anovulation ♒ ♒....... very important**

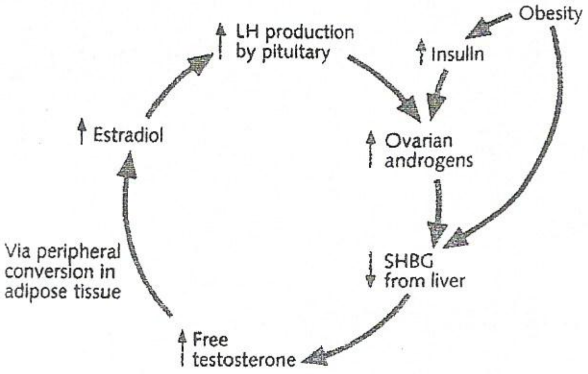
➡ **Tests for etiology ♒.......e.g.**

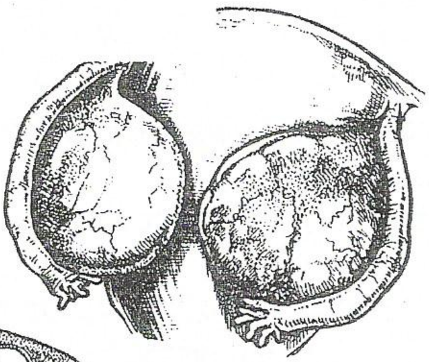
1. Thyroid function tests & prolactin level
2. PCO → LH / FSH ratio
3. Testosterone level → virilizing ovarian tumors
4. DHEA-S level → adrenal origin

Treatment

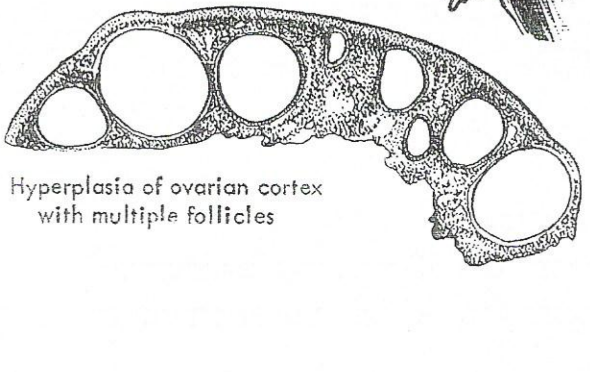
- General → correction of malnutrition, anemia, DM
- Medical → induction of ovulation, bromocriptine if hyperprolactinemia
- Surgical → ovarian drilling for PCO, surgery for virilizing ovarian tumor







Polycystic ovaries



Hyperplasia of ovarian cortex with multiple follicles

1- PolyCystic Ovarian Syndrome

(*Stein Leventhal Syndrome* -1935)

Definition

. A syndrome ccc by ⇔ ov. dysfunction & loss of normal hormonal cyclicity
. Presented by ⇔ **Infertility, Obesity, Hirsutism, Anovulation**

Prevalence

. Affects 5–10 % of females in the reproductive age
. It is the commonest ✓ ovarian cause of 2ry amenorrhea, chronic anov & infertility
. Etiology is unclear ± FAMILIAL & GENE TENDENCY

Pathophysiology

▸ **A vicious cycle, may start anywhere:**
- Primary CNS error ⇔ hypothalamus, pituitary
- Primary endocrinological (enzymatic) error ⇔ ovary, adrenal, liver

▸ **There is high LH pulse / frequency**
↘ stimulates androgen formation by theca cells & ovarian stroma
↘ Inhibits aromatase enzyme (responsible for conversion of androgen into E_2)

▸ **This will result in hyperandrogenism, leading to**
↘ arrest of follicular development at various stages + thick capsule
↘ multiple subcapsular cysts but with no CL → anovulation & infertility
↘ peripheral conversion of the high androgen to E_1 (in fat)

▸ **This acyclic increase in E_1 leads to**
↘ +ve feedback on LH & –ve feedback on FSH → () vicious cycle ()
↘ stimulation of endom→ prolif→ amen & bleeding→ hyperplasia→ cr ¤

> ψ **Associating insulin resistance is found in 40% of PCO**
> ↑ local ovarian ILGF stimulation of androgen synthesis
> Androgens 1......→ ↑ insulin resistance furthermore
> 2......→ ↓ SHBG → ↑ free E & An furthermore
> 3......→ central obesity → ↓ SHBG furthermore

Pathology

* Uterus............................unopposed E → symmetrically enlarged
→ adenomyosis ± end. hyperplasia

* Ovaries..........................(*polycystic, sclerocystic*)
- Size ⇔ enlarged 2–4 times
- Tunica albuginea ⇔ thick, ivory white, smooth (no stigma of ovulation)
- Cysts ⇔ multiple, small, subcapsular filled with clear fluid (rich in E+A)
- Stroma ⇔ hyperplasia of theca & stroma cells (stromal hyperthecosis)

Diagnosed by

❶ Suggestive clinical picture

▸ **Symptoms** ...... *a variable scope of C/P (SOHA)*........

- Anovulation (periods of amen /oligohypom → PPI bleeding)
- Infertility ± habitual abortion (probably d.t. the high LH)
- Hirsutism & acne (hyperandrogenism) – 70%, acanthosis nigricans
- Obesity – 50%: (obesity = BMI > 27 kg/m^2)

▸ **Signs**

- Symmetrically enlarged uterus
- Bilateral enlarged ovaries

❷ Ultrasonic criteria suggestive of PCO

. Necklace appearance (≥ 10 subcapsular cystic follicles) } **Adams**
. Each cyst is 2–10 mm in diameter → microcysts } **criteria**
. The whole ovarian volume is increased > 10 cm^3 }

▸ **By laparoscopy** ➡ large ovary with *smooth* white capsule

.......These findings are <u>Normal</u> in 25% (**polycystic like ovaries**) As it may occur in any case of *prolonged anovulation* + *hyper* 'E'

❸ Specific hormonal changes

- ⇧ LH, ⇩ FSH............................LH/FSH ratio ≥ 2.5 ✓✓
- ⇧ Androgens (testosterone, androstenedione, DHEAS) ✓✓
- ⇧ Estrogens (E_1 mainly)
- ⇧ Prolactin (<30 ng/ml)
- ⇧ Insulin → hyperinsulinemia (fasting glucose / insulin ratio < 4.5)

▸ ⇩ **Progesterone** (mid-luteal)...............*anovulation* ♒ ✓✓

Complications Φ .... *long term risks* ....

- D&C → **endometrial hyperplasia** ± **carcinoma**
- GTT → **DM**
- HDL, LDL, cholesterol → **CVD**

Diagnosed by ....2 *or more of*............

- C/P.....Chronic anovulation ⇨ 2^{ry} amenorrhea / oligomenorrhea } **Rotterdam**
- U/S......Ultrasonic criteria ⇨ suggestive of PCO } **criteria**
- Horm...Hyperandrogenism ⇨ hirsutism, ⇧ LH, ⇧ free testost. } –recent–

Treatment .... *According to C/O* ....

1] **Weight reduction** ✓✓✓ ➡ ⇩ hyperinsulinemia & hyperandrogenism

2] **If the main complaint is hirsutism**

- COC......containing 3rd generation 'P' e.g. Yasmin/ Gynera/ Marvelon/ Cylest
- Diane.....35μg EE + 2mg cyproterone acetate

3] **If the main complaint is irregular uterine bleeding**

- Medical
  - COC: 21 days → stop 7 days → repeat
  - Progesterone
    - Provera (medroxy progesterone acetate) 10 mg
    - Prevents also end. hyperplasia d.t. unopposed 'E'
- D & C
  - *Therapeutic* → if medical therapy failed
  - *Diagnostic* → to exclude endometrial hyperplasia & malignancy
- Hysterectomy
  - *Atypical hyperplasia* OR *Endometrial carcinoma*
  - In *old patient* → with failed medical therapy and D&C

4] **If pregnancy is desired**

- Medical
  - Induction of ovulation
  - Oral hypoglycemics ✓✓✓ metformin (glucophage) 500 mg 1x3
    - ↓ insulin resistance → ↓ androgens → spontaneous preg.
- Surgical ➡ if failed induction

  * Laparoscopic ovarian drilling
  . 4-8 punctures in each ovary for 2-4 seconds each
  . Advantages → less adhesions:- pregnancy rate 70 %

  > *Mechanism of action of surgical drilling* (unknown, m.b.d.t.)
  > - Removal of the thick tunica → allows the follicles to rupture
  > - Removal of part of theca cells → reduction of androgens
  > - Removal of the ↑ed ovarian tension → correction of local factors
  > - Removal of a large part of the ovary → allows better GnRH control

  * Bilateral wedge resection XXXX
  . Removal of ¼ or ½ of the ovary
  . Disadvantage → more adhesions:- pregnancy rate 50 %

- ART ➡ if failed all other measures

2- HyperProlactinaemia ✍

Prolactin

* **Chemistry** → alcohol soluble polypeptide hormone ¤
* **Source** → anterior pituitary lactotropes (acidophils) → *lactotrophic hormone*
* **Function** → prepares the breast for milk secretion, inhibits ovulation (how?)
* **Normal Level**
  . 2 – 25 ng/ml
  . Present in 3 forms (small✓✓.........big........big big)
  . Secretion is variable ∴ measured 3 times at least
* **Control** → prolactin inhibiting factor (dopamine) from hypothalamus
* **Galactorrhea**
  . Any persistent discharge from the breast except *blood* or *pus* in absence of lactation. It is more commonly *bilateral* ¤
  . Diagnosed by mic. ✓ examination (fatty) + Sudan III stain
  . Hyperprolactinaemia in males → galactorrhea & impotence

Etiology ΦΦΦ

▸ **Hypothalamic** ➟ tumors destroying the inhibitory pathway

▸ **Pituitary** ➟ prolactinoma (pit. adenoma) → THE COMMONEST (50%) ✓✓

▸ **Ovarian** ➟ PCO (prolactin ↑ to 30 ng/ml due to ↑ E)

▾ **Idiopathic (physiological)**
  . Pregnancy → up to 400 ng/ml (due to estrogen)
  . **S**uckling (lactation) → up to 200 ng/ml
  . **S**tress / **S**leep / **S**exual intercourse
  / **S**ome emotional disturbances

▾ **Iatrogenic (antidopaminergic drugs)**
  . Estrogen & COC
  . **Anti**depressants & tranquilizers → diazepam
  . **Anti**emetics → metoclopramide (PRIMPERAN)
  . **Anti**hypertensives → reserpine, α-methyl dopa ¤

▾ **Chronic diseases**
  . Hypothyroidism → ↑ TRH → stimulates lactotropes ¤
  . Chronic renal or hepatic failure (↓ prolactin metabolism) ¤
  . Chronic irritation of nipple → burn, scar, herpes zoster
  . Ectopic secretion → oat cell carcinoma of lung ¤

Clinical picture ....(AMENORRHEA-GALACTORRHEA SYNDROME)..........

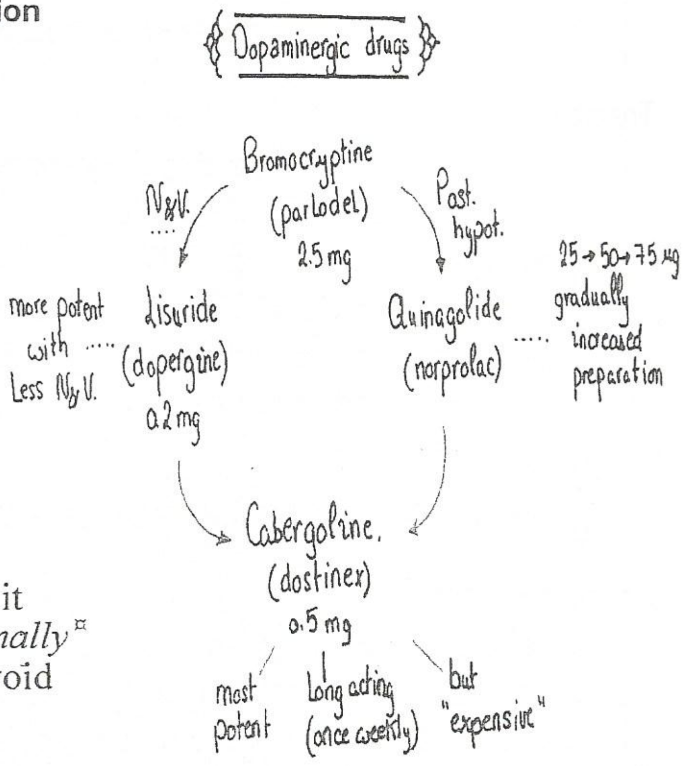
1. **Anovulation** → amenorrhea, oligomenorrhea, DUB } **leads to**
2. **Luteal phase defect:** as prolactin → ↑ luteolysis } **Infertility**

3. **Galactorrhea** → only in 30- 60 % of hyperprolactinaemia
   Premenstrual syndrome
4. **Hirsutism** (prolactin → ↑ adrenal androgens)

± **Manifestations of pituitary tumors** (e.g. ↑ ICT, visual field defects)

Investigations

- **Exclude** ⇒ *pregnancy, lactation........drugs.........thyroid function tests*
- **Prolactin level** ⇒
  - 30 ng/ml..............PCO (U/S + LH / FSH ratio)
  - < 100 ng/ml......... most probably not a tumor
  - 100-200 ng/ml........may be a tumor or not
  - 200 ng/ml..............almost diagnostic of tumor
- **For etiology** ⇒ **CT scan (MRI better):** macro (>1) or micro (<1) – adenoma
  + **Visual field examination**



Treatment

1. **Treatment of the cause**
   → hypothyroidism or renal failure
2. **Stop any causative drug**
3. **Bromocriptine (Parlodel)**
   ✓✓ → dopamine agonist
   * It is an ergot alkaloid ¤
   * Dose: 2.5 mg tablet twice daily
   * Side effects:
     . N&V → avoided by giving it with meals or *vaginally* ¤
     . Postural hypotension → avoid by gradual ↑ of dose
4. **If tumor (Pituitary adenoma)**
   * Dopaminergic drugs forever → satisfactory results (⅓ disappear spont. ¤)
   * Indications of surgery
     . Tumor doesn't ↓ in size with drugs
     . Vision is affected (compression of optic chiasma)
     . Intolerable side effects of the drugs
5. **If got pregnant**
   * Continue dopamine agonists ¤ (not teratogenic)
   * Follow up the visual field / trimester

3- LUTEAL PHASE DEFECT (LPD)

Definition

Inadequate progesterone in the luteal phase leading to

- 4% of infertility cases
- 35% of repeated abortions

Etiology

1. **Defect in CL function**
   - Normally in → post-menarcheal, post-delivery, pre-menopausal
   - Reduced follicular maturation (↓ FSH & LH.....pit or hypothalamic)
2. **Early degeneration (luteolysis) of CL**
   - Endometriosis (↑ $PG\text{-}F_{2\alpha}$)
   - Hyperprolactinemia, Hyperandrogenism, Hypothyroidism
3. **Endometrial insensitivity to progesterone**

Diagnosis + tests for ovulation

. *Premenstrual spotting* ⇒ irregular ripening of endometrium

. *Biphasic body temp* ⇒ short < 10 days

. *Midluteal serum progesterone* ⇒ 3-12 ng/ml

. *Premenstrual endometrial biopsy* ⇒

- lag ≥ 2 days in endometrial development } poor secretory
- "Out of phase when compared to normal" } changes

Treatment

- Prog. in the 2nd ½ of the cycle ⇔ continue by DMPA IM/wk for 10 wks if preg.
- HCG in the 2nd ½ of the cycle
- Induction of ovulation....
  - Clomid ± HCG
  - Clomid ± parlodel or thyroxine or steroids
  - Gonadotrophins + HCG

4- LUTEINIZED UNRUPTURED FOLLICLE (LUFS)

Pathogenesis

. Failure of rupture of the mature GF (probably due to PG imbalance)

. This is followed by luteinization of cells → progesterone secretion

. The resultant is → NO ovulation in the presence of ADEQUATE luteal phase

Diagnosis

- Tests for LPD –ve
- Follow up of GF by U/S → no collapse of follicle

Treatment

Proper induction of ovulation + give *high dose HCG* at ovulation time

5- PREMATURE OVARIAN FAILURE (POF)

Definition ⟹ cessation of menses < 40 yrs due to depletion of follicles (1%)

Etiology........did by CIA ΦΦ

1. Destruction by
   . Chemotherapy
   . Radiotherapy
   . Hysterectomy
2. Idiopathic ⟹ commonest ✓ (+ve family history)
   – helped by smoking, alcohol, undernourishment –
3. Debilitating disease ⟹ pernicious anemia ¤
4. Chromosomal ⟹Turner, trisomy 18 or 13
5. Infections ⟹ mumps?, TB
6. Autoimmune ⟹ anti-ovarian antibodies → lymphocytes & plasma cells surrounds the follicles e.g. Hashimoto thyroiditis

Diagnosis

- **History** → amenorrhoea < 40 yrs (take care ……pregnant? ……!!) ☺
- **C/P** → of estrogen deficiency (as hot flushes)
- **Investigations**
  - FSH > 25–40 mIU /mL (hypergonadotrophic-hypogonadism)
  - Chromosomal → Turner syndrome
  - Ovarian biopsy:
    . POF → no follicles
    . Autoimmune → lymphocytes & plasma cells
    . Resistant ovary syndrome → normal number of follicles

TTT ⟹ **HRT:** ↓ risk of CHD & osteoporosis

6- RESISTANT OVARY SYNDROME (Savage syndrome ¤)

Pathogenesis

- Failure of the ovary to respond to pituitary Gn
- d.t. absence of Gn receptors in ovary or presence of antibodies

Investigations

- ↓E + ↑FSH (hyper-gonadotrophic hypo-gonadism)
- Ovarian biopsy → normal follicles (to differentiate it from POF)

Treatment

- Spontaneous recovery may occur
- Induction of ovulation is VERY difficult (needs large doses of Gn)
- Oocyte donation (condemned ?)

7- HYPERANDROGENISM

Etiology ΦΦ

❶ ⇧ **androgen production**

- ▸ **Endogenous**
  - *Ovary*..............PCO (2^{nd} common) **or** virilizing tumor
  - *Adrenal*............CAH, Cushing synd. **or** virilizing tumor
- ▸ **Exogenous** → anabolic steroids, some progestogens, danazol

❷ ⇩ **androgen binding** ➡ due to ⇩ SHBG

- ▸ Liver diseases (SHBG is synthesized in liver)
- ▸ Hypothyroidism, acromegaly, obesity, insulin resistance
- ▸ Hyperprolactinemia, hyperandrogenism

❸ ⇧ **sensitivity of hair follicles** to normal T levels } *idiopathic*,
or ⇧ **5α-reductase activity** (converts T to DHT) } *constitutional*

- ▸ Commonest cause ✓
- ▸ Menstruation is regular & androgens level is normal

Clinical picture

1. Hirsutism (Ferriman Gallwey scoring system)

- Growth of terminal (sexual) thick pigmented hair mainly in central areas
  - ς early age of onset suggests → familial tendency
  - ς rapid rate of progression suggests → tumors
- *Hypertrichosis* is growth of villus (non-sexual) thin & unpigmented hair

2. Virilization signs

- Acne, seborrhea, temporal baldness
- Skeletal muscle hypertrophy, deepening of voice
- Clitromegaly, increased libido, menstrual irregularities

3. C/P suggestive of etiology

- Family history of hirsutism
- History of drug intake
- Galactorrhea, hypothyroidism
- Swelling:
  - * Abdominal → adrenal tumor
  - * Pelvic → PCO, ovarian tumor

Investigations

- **Exclude** ➡ *family history........drugs........thyroid function tests*
- **Testosterone level** ➡
  - If normal.... 0.2–0.8 ng/ml ......no further investigation (idiopathic)
  - If testosterone > 150-200 ng/dl (N: 20-80)...ovarian tumor.......U/S
  - If DHEA-S > 700 μg/dl (N: 150-300)...........adrenal tumor.......CT
- **For etiology**
  - U/S + LH/FSH ratio ≥ 3 → *PCO*
  - Serum prolactin → *hyperprolactinemia*
  - Serum cortisol & serum DHEAS → *Cushing synd.*
  - Serum 17α- OH progest. → *CAH*

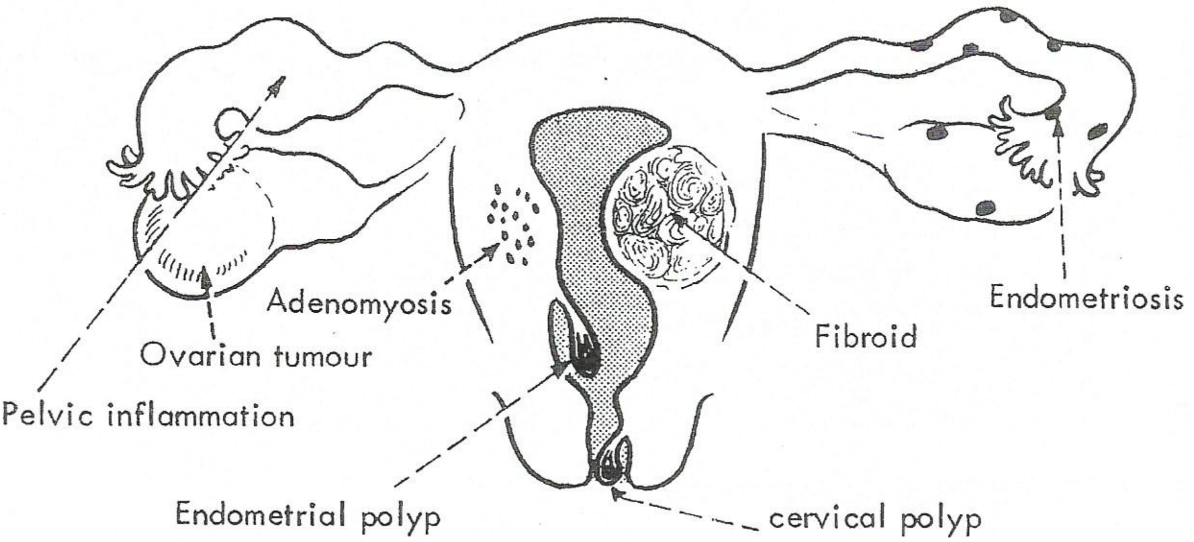
Treatment

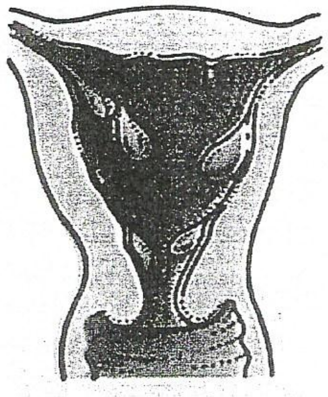
1. **Treatment of the cause** e.g. laparoscope for PCO
2. **Cosmetic treatment** e.g. shaving, depilation, waxing, laser
3. **Drugs** ➡ the response to treatment is slow (after 6-9 months) as hair life cycle is slow. ∴ drugs given for 1–2 yrs

Androgen secreting glands			Peripheral	Central
OVARY		ADRENAL		
❶ **Estrogen**	❷ **Progest.**	❸ **Dexamethasone**	❹ **Flutamide** blocks androgen receptor (eulexin 250 mg/day)	❻ **GnRH analogues**
↑ synthesis of SHGB → ↓ free androgen e.g. - *Yasmine* - *Gynera* - *Cilest*	↓ LH secretion → ↓ ovarian Androgen e.g. . *Provera* (10mg/d) . *DMPA IM* (150 mg /3m)	0.25–0.5mg / day → suppress the adrenal gland	❺ **Finasteride** (proscar) inhibits 5α-reductase enz. (5mg/d)	↓ ovarian E & A → amenorrhoea (but leads to osteoporosis within 6 m)

Others (important)

- *Androcur* (cyproterone acetate) → progestogenic & antiandrogenic
- *Spironolactone* ✓ ✓ (aldactone) 25 mg /d → acts as androcur
- *Diane* → 35μg EE + 2 mg cyproterone acetate





Uetrin polyps

Abnormal Genital Bleeding

Definitions

1) Cyclic bleeding
   - Menorrhagia (excessive *amount / duration* at time of menses)
   - Polymenorrhea (too frequent menstruation d.t. too short cycles)
   - Polymenorrhagia (combination of the above)
2) Acyclic bleeding
   - Metrorrhagia (irregular bleeding unrelated to menstrual cycles)
   - Menometrorrhagia
   - Intermenstrual bleeding

Organic

A) General

- **Increased bleeding tendency**
  - Blood diseases affecting coagulation e.g. VWD, ITP
  - Hypertension, Congestive heart failure
- **Organ failure** ⇨ renal / liver (↓ E metabolism, ↓ SHBG, ↓ clotting factors)
- **Endocrine** ⇨ adrenal / thyroid disorders (↓ or ↑)…DM (vasculopathy)
- **Drugs** ⇨ antiplatelet, anticoagulants, contraceptive drugs

B) Local ΦΦ

- *Complications of pregnancy :-*
  - ***Early*** ~ abortion, ectopic, V.M.
  - ***APhge*** ~ placental, extraplacental
  - ***PPhge*** ~ atonic, traumatic, retained placenta, DIC
- *Pelvic pathology :-*

1] ***Congenital*** ⇨ uterus didelphys / bicornis → menorrhagia

2] ***Traumatic*** ⇨ obstetric, surgical, direct…………..IUCD

3] ***Inflammatory*** ⇨ acute / chronic infection → ulcers & pelvic congestion

4] ***Tumors*** ⇨
   - Cervix (benign → **polyp 10%** ~ malignant → carcinoma or sarcoma)
   - Uterus (benign → **fibroid 30%** ~ malignant → carcinoma or sarcoma)
   - Endometriosis & adenomyosis
   - Ovary (neoplastic or non-neoplastic)

5] ***Genital displacements*** ⇨ prolapse, RVF, chronic inversion of uterus

❋ Dysfunctional (functional)

DEFINITION

- Abnormal uterine bleeding in absence of obvious ORGANIC cause
- Common near . Puberty (immature HPO axis).............20%
  . Menopause (reduced no of follicles)......40%
- Due to
  . Hormonal dysfunction (HPO axis)......Metrorrhagia (80% of DUB)
  . Local end. defect (PG imbalance).......Menorrhagia (20% of DUB)
    - PG E_2 & Prostacyclin
    - PG $F_2\alpha$ & TXA_2

A) Ovular (cyclic) ➡ menorrhagia

excessive amount / da
⇓
cycles are very sh

↳ Functional Polymenorrhea & Polymenorrhagia

- The cycles are very short (d.t. short follicular phase)

(ripening) ↳ Irregular ripening of endometrium (CLI, LPD)
pre

- Poor formation of CL → premature shedding of endometrium → premenstrual spotting

(shedding) ↳ Irregular shedding of endometrium
↳ post

- Incomplete & slow degeneration of endometrium → postmenstrual spotting

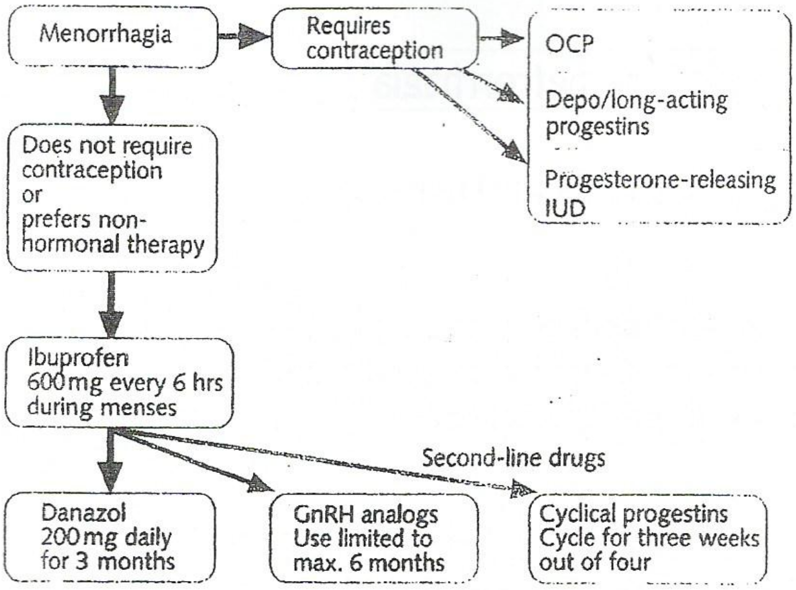
↳ Halban's disease (Persistent CL)

- (Unknown etiology) but there may be → PG imbalance in ovaries (PG is important for luteolysis) → abnormal uterine bleeding
- DD is ectopic pregnancy ~ differentiated by β-HCG

Treatment for all...........

* IF BLEEDING
- Progesterone (e.g. provera or primolut 10 mg/d)
- COC → inhibits pituitary & start artificial cycles

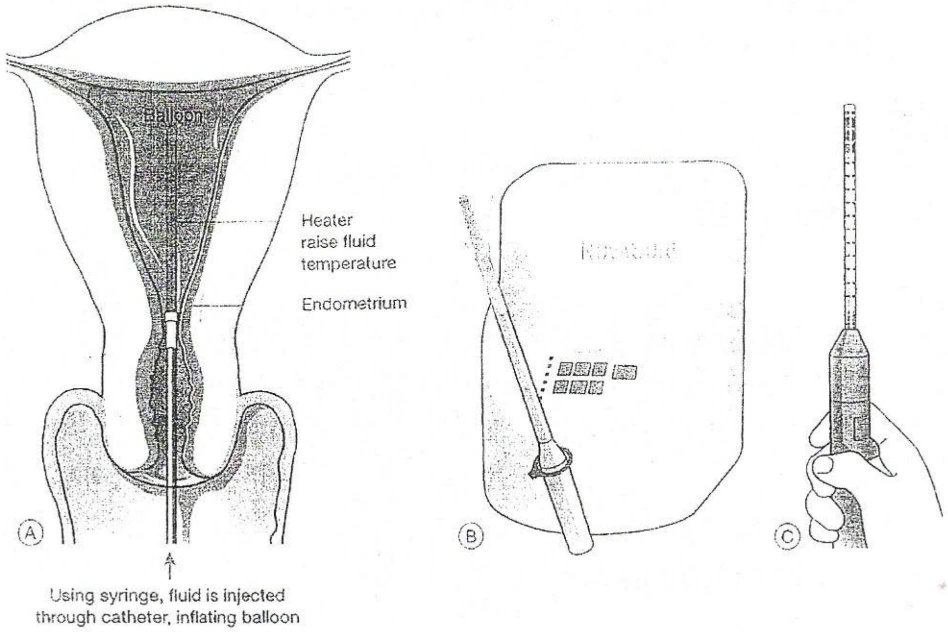
* IF INFERTILITY
- HCG or clomid + HCG
- ART → if failed induction



Algorithm for menorrhagia.

Hysteroscopic view of intrauterine polyp.

An intrauterine progestogen-releasing system in the uterus.



Conservative surgical treatments for menorrhagia. (A) A thermal balloon; (B) impedance-controlled ablation; (C) microwave endometrial ablation.

▸ Treatment

1- ***General***

- Correct anemia (even blood transfusion may be required)
- Anti-PG ✓✓ e.g. Mefenamic acid, Ponstan, ibuprofen
- Anti-fibrinolytics e.g. tranexamic acid (*cyklokapron*)
- Haemostatics e.g. diosmin (*daflon*), ethamsylate (*dicynone*)

2- ***Hormonal***

- If Bleeding
  - ➡ **Progestins**
    - Provera 10 mg/d for 21
    - LNG-IUS (Mirena) ✓✓ → ↓ bleeding 90% in 1 yr
  - ➡ **COC**
    - Once daily: 21 days → stop 1 wk → repeat
- If failed
  - ➡ Danazol or Dimetriose (gestrinone)
  - ➡ GnRH analogues
- If infertility........induction of ovulation

3- ***Surgical***

- D&C → diagnostic (ovular or not ~ tumor or not) & therapeutic...50%
- Hysteroscopic endometrial ablation
  - ➡ 1st generation....endometrial loop resection / diathermy / laser
  - ➡ 2nd generation...microwave / radiofrequency ablation (novasure) ✓✓
- Hysterectomy –vaginal, abdominal, laparoscopic–
  - ➡ Failed all above measures to stop bleeding
  - ➡ Associating pathology is found
  - ➡ Old age

> **NB: In Acute bleeding episodes**
> * Hospitalization & resuscitation (2 wide bore cannula)
> * High doses of ⇨ Estrogen [CEE 25 mg IV / 4 hrs] or COC [1 x 4 x 5]
> * Emergency D&C

2] Threshold Bleeding

▸ Etiology

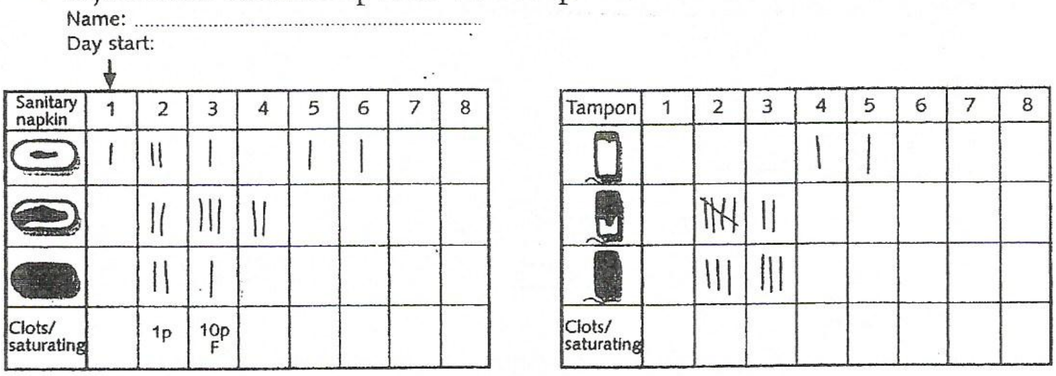
Occurs at extremes of reproductive life due to waxing & waning of estrogen levels which are high enough to stimulate proliferation but not to maintain it

▸ Treatment

- Estrogen for 10 d. then → E+ P for 10 d. → repeat for 3 cycles
- Induction of ovulation if infertility

---Types of bleeding according to hormonal action---

- *Withdrawal* (E + P)
  - Normal menstruation
  - After COC
- *Breakthrough*
  - E → metropathia haemorrhagica
  - P → injectable contraception or Norplant



Pictorial blood-loss assessment chart.

---Types of bleeding according to pattern---

↪ ***Menorrhagia*** (now known as HMB = heavy menstrual bleeding)

- Local ....fibroid, endometriosis, PID
- Systemic...........blood disorders
- DUB..............irregular ripening or shedding

↪ ***Polymenorrhea***

- Local ....ovarian congestion (endometriosis, PID)
- Systemic..........
- DUB.............functional polymenorrhea

↪ ***Metrorrhagia***

- Local ....benign/malignant neoplasms, cervical ulcers
- Systemic..........irregular use of contraceptives, IUCD
- DUB.............metropathia haemorrhagica

↪ ***Contact bleeding***

- Cervicitis.........cervical ulcers (erosion)......cervical ectopy
- CIN..............cancer cervix
- Vaginal or uterine tumors bulging into vagina
- Severe vaginitis esp senile type

> Contact bleeding is considered CIN until proved otherwise

... Abnormal genital bleeding according to age ...

↪ *Neonatal period*

Slight bleeding may occur in the 1st week → birth crisis d.t. withdrawal of 'E' obtained from maternal circulation

↪ *Childhood......* ✍

- Traumatic → foreign body ✓, sexual abuse
- Inflammatory → Pre-pubertal vulvovaginitis ✓✓
- Neoplastic → . Sarcoma botryoids (cervix or vagina)
  . Germ or Granulosa cell tumor (ovary)
- Miscellaneous → Precocious puberty

↪ *Puberty*

- Dysfunctional uterine bleeding
- Coagulopathies (VWD)

↪ *Childbearing period*

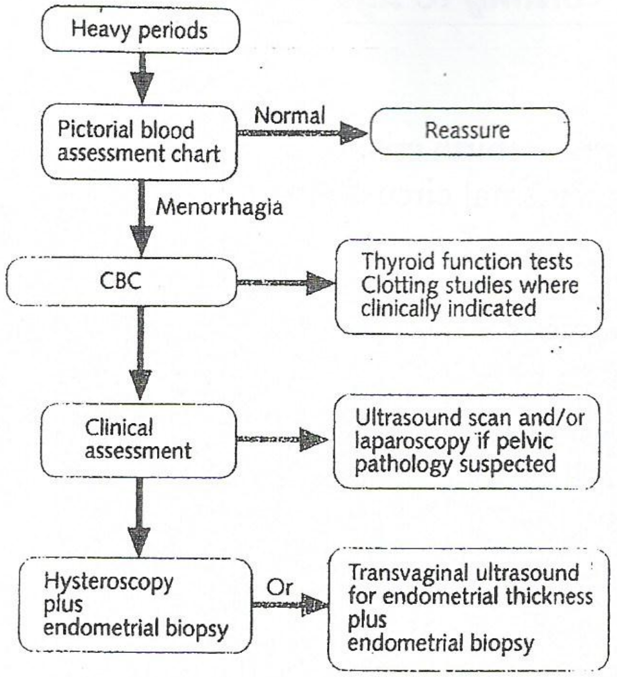
- Complications of pregnancy
- Complications of contraception

↪ *Perimenopausal bleeding......* ✍ ΦΦ

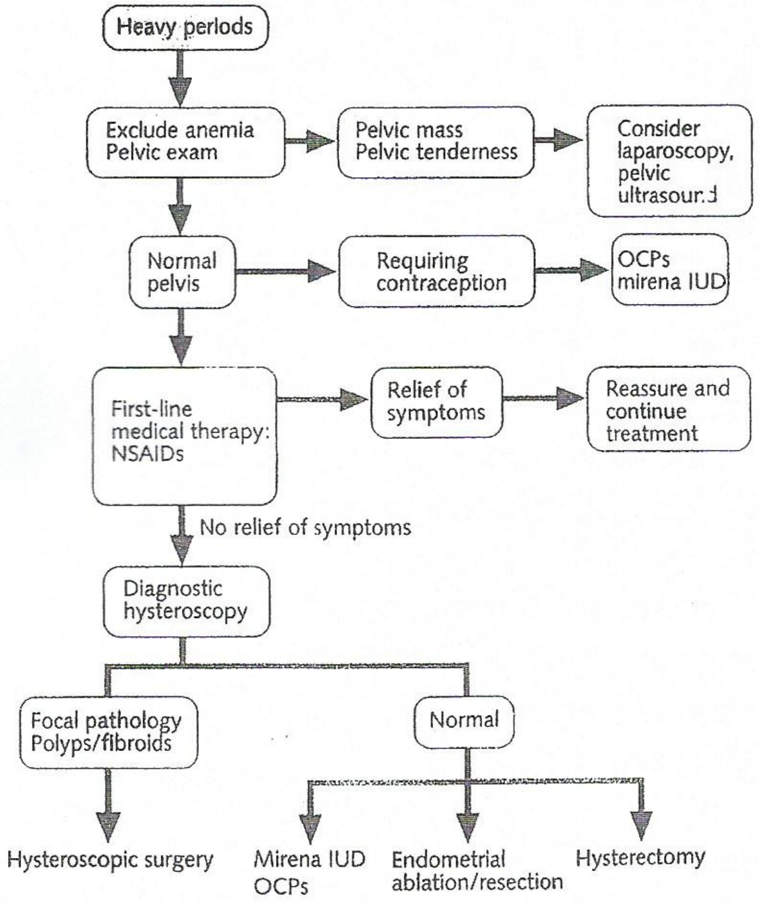
- Dysfunctional uterine bleeding
- Organic → incidence of tumors is increased (e.g. fibroid, CIN)

↪ *Postmenopausal bleeding.......* ✍ ΦΦ

- Malignant tumors of genital tract y
  - The most serious but not the most common (risk is 10–20 %)
  - Endometrial carcinoma....cervical cancer.....others
- Benign conditions of genital tract
  - Tumors → endometrial hyperplasia, fibroids, polyps ✓
  - Atrophic (*senile*) endometrium..........✓(ttt by HRT)
  - Postmenopausal atrophic vulvo-vaginitis
- Complications of HRT or Prolapse:-
  - Trophic ulcers
  - Neglected retained pessary
- Non-gynecological conditions
  - General.................hematologic diseases, severe hypertension
  - Bleeding / urethra......urethral caruncle
  - Bleeding / rectum......piles or malignancy



Investigating menorrhagia.



Algorithm for abnormal uterine bleeding.

How to approach a case of abnormal genital bleeding ✍

▸ History

- *Age*..................
- *Marital status*........complications of pregnancy
- *Present history*........
  - ➠ Analysis of bleeding ⇔ onset, duration, amount, ccc, ttt received
  - ➠ Exclusion of a pelvic pathology
    - Pain, bleeding, infertility → endometriosis
    - Something protruding → prolapse
    - Fever, pain , offensive discharge → PID
- *Menstrual history*.....to see if cyclic or acyclic
- *Obstetric history*......recent abortion (2^{ry} hge), recent VM (choriocarcinoma)
- *Contraceptive* ....irregular COC intake, long acting injectables
- *Past history*...........hypertension, endocrine disease, easy bruises

▸ Examination

- *General*
  - Anemia & its degree
  - General disease e.g. hypertension, endocrinological disease
  - Metastasis & jaundice
- *Abdominal*
  - Pelviabdominal swelling (fibroid, ovarian tumor)
  - Pregnancy
- *Vaginal* → detect a local cause ± P/R

▸ Investigation

- *Blood tests*
  - CBC, coagulation profile ✓✓
  - Organ function test (etiology or preoperative preparation)
  - Hormonal assay (for DUB)
  - Tumor markers
- *Scanning*
  - X-ray (chest, HSG)
  - U/S (abdominal, vaginal), CT, MRI
- *Endoscopy* → Laparoscopy, hysteroscopy, colposcopy
- *Biopsy* - Endometrial sampling
  - Cervical biopsy
  - Vaginal cytology

KEY POINTS

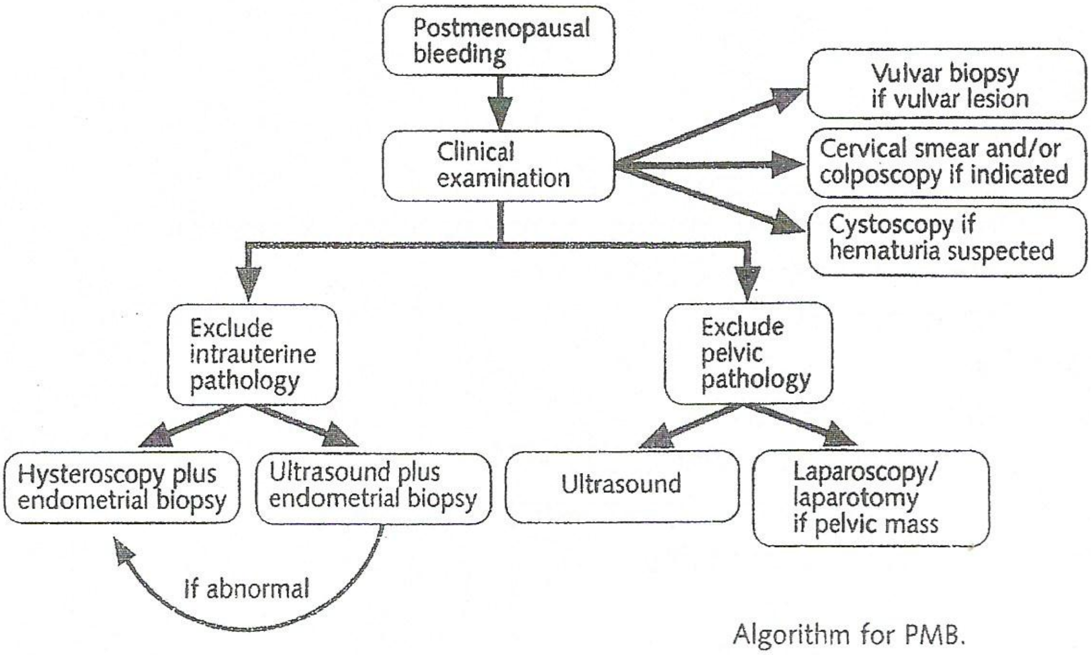
1. DUB is a diagnosis of exclusion when no other source for abnormal bleeding can be identified.
2. DUB is thought to be secondary to anovulation, and is therefore more prevalent near menarche and menopause.
3. Treatment includes initial medical therapy but may require surgical modalities for those patients whose symptoms are not controlled with medical management.

KEY POINTS

1. The most common cause of oligomenorrhea and secondary amenorrhea is pregnancy.
2. Structural abnormalities—polyps, fibroids, adenomyosis, and cancer—cause most of the menorrhagia, metrorrhagia, and menometrorrhagia except that which is related to pregnancy.

KEY POINTS

1. Postmenopausal bleeding should always be investigated to rule out cancer.
2. Causes of postmenopausal bleeding include cancer of the upper and lower genital tract, endometrial polyps, exogenous hormonal stimulation, vaginal atrophy, and nongynecologic sources.



Algorithm for PMB.

Discuss post–menopausal bleeding

- **Definition** ⟹ bleeding from genital tract 1 year after menopause
- **Etiology** . Risk of malignancy is 10 – 20 %
  . PMB is considered malignant until proved otherwise
- **History**
  - *Age*......... post-menopausal
  - *Race*.........endometrial cancer more common in white race
  - *Present history*........
    - ⟹ Analysis of bleeding ⇔ onset, duration, amount, ccc, ttt received
    - ⟹ Exclusion of a pelvic pathology
      - Pain, swelling → tumor
      - Something protruding → prolapse
      - Pain, dysparuenia, discharge → atrophic changes
  - *Obstetric history*........
    - Low parity → cancer endometrium & ovary
    - High parity → cancer cervix
  - *Past history*............
    - Hematologic diseases, hypertension
    - Hormone intake
- **Examination**
  - *General*
    - General disease e.g. hypertension, hematological disease
    - Metastasis & jaundice
  - *Abdominal*
    - Pelvi-abdominal swelling (ovarian tumor, pyometra in cr. end. / cx)
    - Hepato-splenomegaly (metastasis)
  - *Vaginal* → detect a local cause (in details)
    - Inspection & palpation vulva
    - PV & cusco
    - Bimanual examination
    - PR is very important in tumors
- **Investigation**
  - *Diagnosis* ⟹ U/S, hysteroscope, **biopsy** (D&C or pap), tumor markers
  - *Preoperative* ⟹ CBC, coagulation profile, blood glucose, ECG
  - *Metastasis* ⟹ chest x-ray, CT abdomen
  - *Other causes* ⟹
- **Treatment**............of the cause in short (end.cr., cx.cr)

Dysmenorrhea

(Pain related to menstruation)

1. Spasmodic (1^{RY}) Dysmenorrhea

Definition Colicky pain of uterine origin occurring on 1^{st} day menses
In absence of any ORGANIC pelvic pathology (idiopathic dysm.) e.g.

- *Pelvic pathology*.......examination, U/S
- *Ectopic*.................no cervical motion tenderness
- *Salpingitis*..............cx smear: no chlamydia or gonorrhea
- *Appendicitis*...........no rebound tenderness, normal TLC, ESR

Clinical picture

- ▶ **Type of patient**
  - Occurs only in ovulatory cycles
  - Starts 2-3 years after menarche & improves after age of 25
  - More in virgins & nulliparus (esp if sedentary life)
  - Improved after childbirth (cervical dilatation)
- ▶ **Type of pain**
  - Site ➡ . Lower abdominal colicky intermittent pain
    . May radiate to Lower limbs (L_1 distribution)
  - Time ➡ - 1^{st} day of menstruation with or just before the flow, then...
    - Rapidly ↓ in intensity after 24 hrs (with establishment of flow)
  - May be associated with ➡ $N_{\&}V$, diarrhea, urinary disturbances
    Sweating & facial pallor (↑ PG?)

Etiology unknown (theories)

- ▶ **Excess prostaglandins** (esp $PGF_2\alpha$) as
  - $PGF_2\alpha$ causes painful cont. & explains some associating sympt. ($N_{\&}V$)
  - Progesterone ↑es PG production (∴anovulatory cycles are painless)
- ▶ **Retention of menstrual flow** as in
  - *Obstructive theory* (acute AVF uterus or cervical stenosis)
  - *Hypoplastic theory* (underdeveloped uterus can't expel blood)
  - *Disturbed polarity* (contraction of cervix & isthmus)

Treatment

1) **Medical** ✓✓
   - ▶ **Anti-PG** e.g. Mefenamic acid, naproxen, ibuprofen, aspirin
   - ▶ **Hormonal suppression of ovulation: COC**
   - ▶ **Recently...** glyceryl trinitrite....vasopressin antagonist....sildenafil
2) **Surgical** ✗✗
   - ▶ **D&C** → dilate the pathway & lacerates paracervical sympathetic nerves
   - ▶ **Presacral neurectomy (LUNA)** → interrupts motor nerves

2. CONGESTIVE DYSMENORRHEA

Definition

Continuous dull aching pain in lower abdomen & back SECONDARY to presence of PELVIC PATHOLOGY. Pain is relieved by menstrual flow.

C/P

- Age → usually occurs later in life (> in MP)
- Pain → - Starts few days (3-5) before menses
  - Gradually ↓ with the flow & on lying down
- Associated symptoms → of pelvic congestion:
  Menorrhagia.........polymenorrhea.........vaginal discharge

Etiology **(of pelvic congestion)**

- Congenital → uterine anomalies
- Inflammatory → cellulitis, peritonitis, cervicitis, PID
- Neoplastic → fibroids, ovarian tumors
- Displacement (RVF & prolapse)
- Functional or simple (anxiety, emotional disturbance, sedentary life, constipation, coitus interruptus)

NB: Endometriosis has special ccc of pain → 2^{ry} spasmodic (crescendo)

Treatment

- Treatment of the cause
- Avoid constipation
- Glycerine icthyol suppositories → ↓ pelvic congestion & pain

3. OTHERS

▸ **Membranous dysmenorrhea**

- Painful passage of large endometrial casts during menses of unknown etiology
- Character → . Severe pain in the 1^{st} few days with scanty flow
  . Passage of complete membranous casts or large fragments
  . Followed by relief of pain & increased flow
- TTT→ suppress ovulation (COC pills for few cycles)

▸ **Ovarian dysmenorrhea (Mittleschmertz)**

- Midcycle dull aching pain felt at ovulation in one or both iliac fossa
- Character → . It lasts only for few hours (sometimes 24 hours)
  . It may be associated with N&V (DD → appendicitis)
  . It may be associated with midcycle → discharge / spotting
- TTT→ reassurance + analgesics (inhibition of ovulation if severe)

Premenstrual syndrome (PMS, PMT)

Definition ⇨ cyclic recurrence of *physical / psychological* sympt occurring in luteal phase (few days < menses) & relieved completely after menses

Incidence

- 50 – 80 % of females will report uncomfortable / distressing symptoms
- Severe symptoms occurs in 5 % only → interruption of social life style, drug dependence (**PMDD** = PreMenstrual Dysphoric Disorder)
- Up to 60% with severe PMS have an underlying psychiatric disorder

Etiology ……… *unknown: theories* …………

▶ **Endocrine**

- ↑ E / ↓ P ratio
- ↑ ADH & aldosterone → salt & H_2O retention
- ↑ prolactin → mastalgia

▶ **Central**

- Serotonin & β-endorphins imbalance ✓→
- Psychological & mood disturbance (anxiety or depression)

▶ **Prostaglandins**

- May explain symptoms in some organs (GUT, GIT, URT)

▶ **Diet**

- High salt + low sugar intake
- Vitamin deficiency (B_6, B_1) → cofactors for neuropeptides

Clinical picture: ……*diagnosed for at least 3 cycles*…..

- Presence of CYCLIC sympt at luteal phase (∴ cycles must be ovulatory)
- ABSENT symptoms at follicular phase (i.e. relieved by menses)
- Physical & laboratory examination EXCLUDES organic pathology
- SYMPTOMS: (≈ 150)
  - ▶ *Physical*
    - Mastalgia (pain & congestion of breast)
    - Joint pain, muscle cramps, backache
    - Abdominal distension, N&V, diarrhea or constipation
    - Water retention → edema of face, LL, ↑ body weight
  - ▶ *Psychological*
    - Depression, fatigue, headache, irritability, change in libido

Treatment

1. General

- Reassurance
- Depression → . Tranquilizers & antidepressants
  . Psychotherapy for resistant cases
- Antiprostaglandins → ↓ pain

2. Diet

- Increase sugar intake & decrease salt
- Linolenic acid derivatives (primarose)
- Encourage exercise
- Diuretics: spironolactone (↓ aldosterone)
  25mg 1x3 → ↓ Na & H_2O

3. Mastalgia

- Vitamin B_6 (pyridoxine) 100 mg → ↑serotonin & dopamine
- Dopamine agonists → parlodel or dopergine

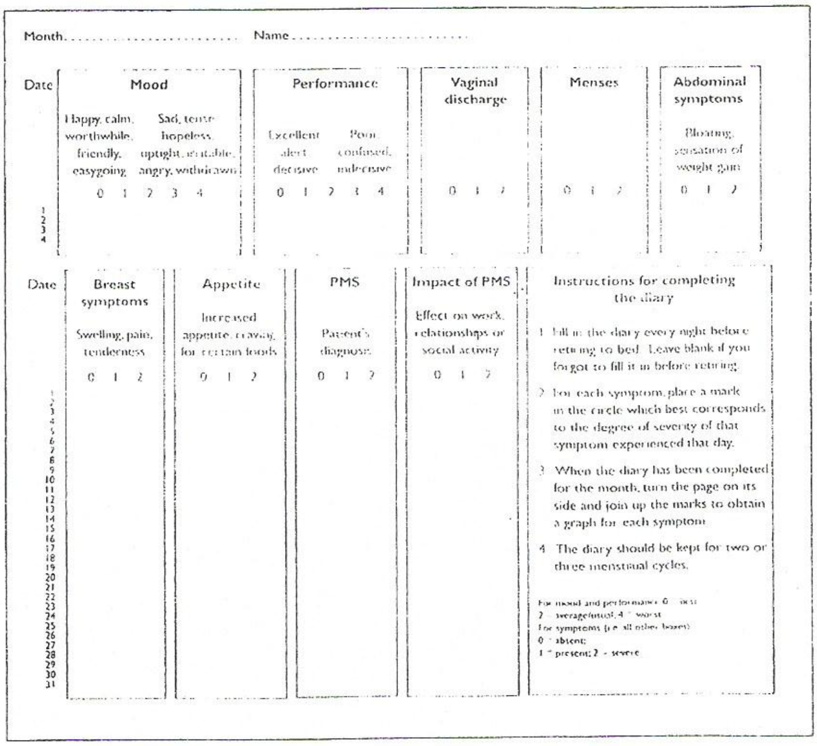
4. Hormones

▶ ***Serotonin re-uptake inhibitor*** ✓✓✓

↘ Fluoxetine is considered now the 1st line ttt for severe PMS

▶ ***Inhibition of ovulation***

- COC (the best ttt)
- Depo-provera (MPA) 150mg IM / 3 m
- GnRH analogues.........osteoporosis on long term
- Danazol } androgenic
- Gestrinone (dimetriose) } side effects
- Mifepristone (RU-486)


Month.......................... Name..........................

Date	Mood	Performance	Vaginal discharge	Menses	Abdominal symptoms
	Happy, calm, worthwhile, friendly, easygoing — Sad, tense, hopeless, uptight, irritable, angry, withdrawn	Excellent, alert, decisive — Poor, confused, indecisive			Bloating, sensation of weight gain
	0 1 2 3 4	0 1 2 3 4	0 1 2	0 1 2	0 1 2
1					
2					
3					
4					

Date	Breast symptoms	Appetite	PMS	Impact of PMS
	Swelling, pain, tenderness	Increased appetite, craving for certain foods	Patient's diagnosis	Effect on work, relationships or social activity
	0 1 2	0 1 2	0 1 2	0 1 2
1–31				

Instructions for completing the diary

1. Fill in the diary every night before retiring to bed. Leave blank if you forgot to fill it in before retiring.
2. For each symptom, place a mark in the circle which best corresponds to the degree of severity of that symptom experienced that day.
3. When the diary has been completed for the month, turn the page on its side and join up the marks to obtain a graph for each symptom.
4. The diary should be kept for two or three menstrual cycles.

For mood and performance: 0 = best; 2 = average/usual; 4 = worst
For symptoms (i.e. all other boxes): 0 = absent; 1 = present; 2 = severe

Menstrual history diary.

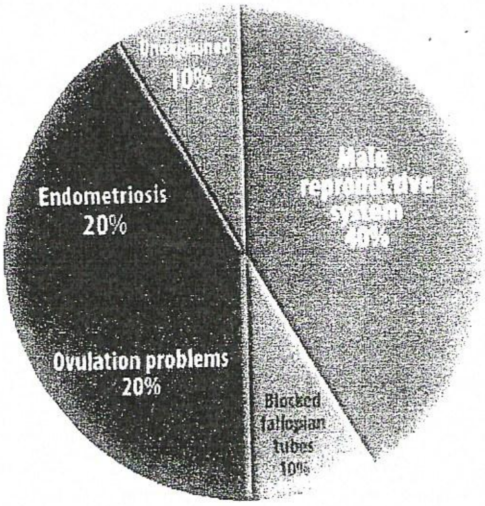
Chapter 3 Infertility

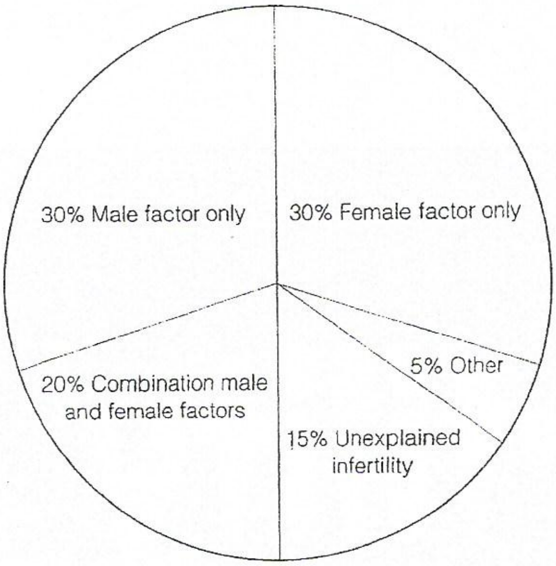
Etiology

Assessment

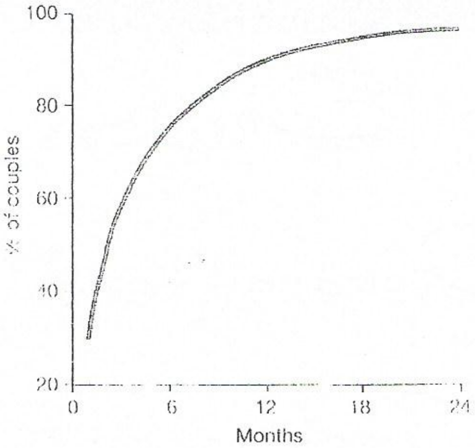
Treatment

Assisted reporoduction





◦ Causes of infertility.



Cumulative pregnancy rates in the normal fertile population.

Infertility

▸ **Definition**

1ry infertility is INABILITY TO CONCEIVE *after* 1 year of continuous marital life *without* use of any contraceptive method

2ry infertility.... PREVIOUS pregnancy occurred (regardless outcome) without using contraception (including lactation)

* Fecundibility ⇨ the monthly probability of pregnancy among fertile couples (20–25 % / cycle in unprotected intercourse)
* Sterility ⇨ irreversible infertility ?
* Start assessment early ⇨ if ❶ previous known disease or ❷ > 35 yrs

▸ **Incidence**

↘ **10 – 15** % (incidence rise with ↑ of **age**)¤
↘ N. conception rate: 20% (1m), 60% (6m), 80% (9m), 90% (12m)

▸ **Etiology** ⟹ (may be ≥ one cause ¤)

A) MALE FACTOR (30–40 %)

❶ Imperfect spermatogenesis

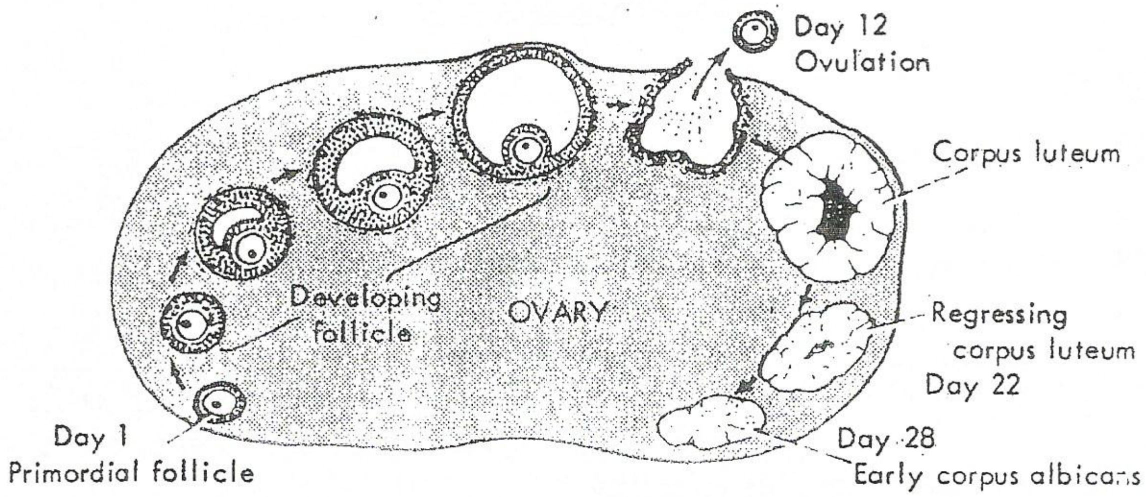
- 1ry testicular failure...high FSH ⇧
  - Congenital → sertoli cell only $, undescended testis, Klinefelter $
  - Traumatic → direct (immunol.), thermal (varicocele → ↓ motility)
  - Inflammatory → mumps orchitis, syphilis
  - Neoplastic → tumors destroying the testis
- 2ry testicular failure (pituitary)...Low FSH ⇩

❷ Obstruction to transport

- Congenital → congenital absence of vas, cystic fibrosis, Kartagener $
- Traumatic → surgery (for hernia or prostate)
- ✓✓ Inflammatory → epididymitis, funiculitis, prostatitis (chlamydia)
- Neoplastic → tumors of epididymis or prostate

❸ Failure of deposition of sperms

- Anatomical → hypospadius & epispadius
- Neurogenic → retrograde ejaculation (diabetic neuropathy & spinal injuries)
  → interference with innervation (known by urinanalysis)
- Psychological → impotence & premature ejaculation



Causes of female infertility

Type of problem	Cause of infertility
Ovulatory problem	Chronic systemic illness
	Eating disorders
	Abnormal pituitary/ hypothalamic/endocrine profile • PCOS • Hyperprolactinemia • Hypo- or hyperthyroidism
	Cannabis use
	NSAIDs
Tubal problem	Previous tubal surgery
	Previous ectopic pregnancy
	Endometriosis
Uterine problem	Submucosal fibroid
	Uterine septum
	Asherman syndrome
	Uterine anomalies
Coital problem	Intercourse not occurring often enough
	Impotence
	Vaginismus

Causes of female infertility.

B) Female Factor (40–50 %)

❶ Ovary (30%) ➡ the commonest cause of 1ry ✓ Infertility

- Group I...... H-P failure..............as in amenorrhea
- Group II..... H-P dysfunction........PCO, idiopathic anovulation
- Group III....Ovarian failure.........Turner $, ROS, POF
- Others
  - *Hyperprolactinemia*...(20 % of ovulatory dysfunction)
  - *Hyperandrogenism*
  - *LPD*.......*Luteal phase defect* (4% of infertile patients)
  - *LUFS*.........*Luteinized Unruptured Follicle Syndrome*

❷ Pelvic (peritoneal)

- *Endometriosis* (10–25% of infertility) } DD of
- *PID (& TB)* } frozen
- *Extensive surgery* } pelvis

❸ Tube (20%) ➡ the commonest cause of 2ry ✓ infertility

- *Congenital*................ hypoplasia, diverticula, accessory ostia
- *Traumatic*....................surgery on or near to the tube
- *Inflammatory*...............salpingitis✓✓
- *Neoplasm*.....................broad lig. fibroid or ovarian cysts

❹ Uterus (5%)

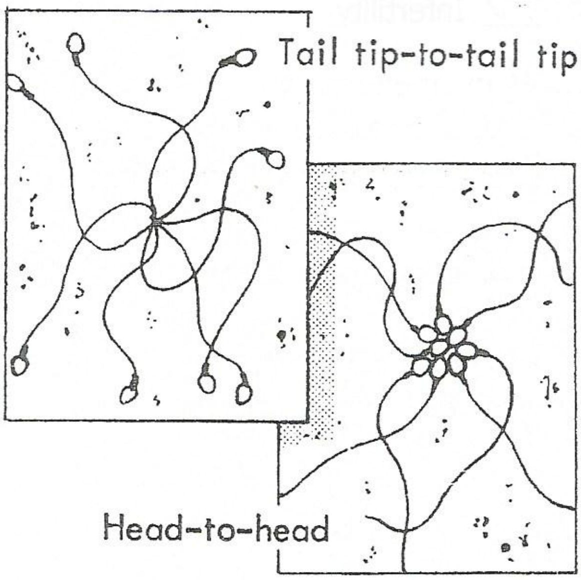
- *Congenital*....................aplasia, hypoplasia
- *Traumatic*....................surgery } Ascherman
- *Inflammatory*...............endometritis } syndrome
- *Neoplasm*...................polyp or fibroid
- *Miscellaneous*...............prolapse & RVF → v. rare

❺ Cervix (5%)

- *Congenital*....................atresia (pin–hole os)
- *Traumatic*....................cautery, cone biopsy } poor hostile
- *Inflammatory*...............chronic cervicitis } cx mucous
- *Neoplasm*.......................polyp or tumor

❻ Vagina

- *Congenital*....................atresia, septum
- *Traumatic*....................previous surgery, stenosis
- *Inflammatory* ....vulvo-vaginitis → hostile to sperms
- *Neoplasm*..................cysts interfering with intercourse



KEY POINTS

1. Between 5% and 10% of couples find no explanation for infertility after their initial assessment.
2. Further assessment may be done to search for problems with sperm transport, ability to penetrate and fertilize the egg, and antisperm antibodies. IVF can be used to treat these patients.
3. Most therapies for unexplained infertility have not been shown to have higher success rates than no treatment.
4. Couples with unexplained infertility who choose no treatment will conceive up to 60% of the time over 3 to 5 years.

C) IMMUNOLOGICAL

- **Antibodies against sperms may be performed in:**
  - *Male* → autoantibodies (after surgery on male genital tract)
  - *Female*
    - Antibodies against blastocyst (IgM) large → serum only
    - Antibodies against sperms (IgG) → formed in cx mucous
- **Antibodies are either:**
  - *Agglutinating* → head to head, head to tail, tail to tail
  - *Immobilizing* → head shakers, rotatory, lost forward motility

D) COITAL (5%)

- **Interference of coitus** → impotence, dyspareunia, vaginismus, anorgasmia
- **Frequency & timing**

  ↓ frequency → decrease chance of conception } best is every
  ↑ frequency → produce immature sperms } other day
- **Use of lubricants & postcoital douching** → kill sperms
- **Effluvium seminis** (escape of semen from vagina after coitus is **normal ?!**)

E) UNEXPLAINED (10–15%)

- **Definition → Infertility in spite of:**
  - Normal **ovulation** (proved by tests for ovulation)
  - Normal **patent tubes** (proved by HSG ± laparoscopy)
  - Normal **uterine cavity** (proved by PEB ± hysteroscopy)
  - Normal **semen analysis** (at least done twice)
  - Normal **postcoital test** (good cx mucus & sperm motility)
- Unexplained infertility in increasing nowadays (up to 15–30 %). It denotes the inability to <u>identify</u> a cause rather than <u>absence</u> of a cause… **Possible causes:-**
  - **Ovary** ➡ *EØ* (75%) → at early stages ∴ laparoscopy ✓
  - **Tube** ➡ *Sperm dysfunction* (inability to attach or penetrate ZP)
  - **Cervix** ➡ *Immunological disorders*
  - **Vagina** ➡ *Subclinical infection* (chlamydia, mycoplasma)
- **Treatment**
  - Induction of ovulation (± bromocriptine ± antibiotics)
  - If failed → AIH
  - If failed → ART

Drugs that Decrease Semen Quality and Quantity

Cimetidine	Nitrofurans	Anabolic steroids
Sulfasalazine	Erythromycin	Chemotherapeutic agents
Spironolactone	Tetracyclines	Heavy marijuana/ alcohol use

Examination of a man

Examination	Reason
Scrotum	Varicocele
Size (volume) of the testes	Small testes associated with oligospermia
Position of the testes	Undescended testes
Prostate	Chronic infection

Abnormalities...OTA...Repeat after 2-3 m

- **Abnormal number**
  - No semen → aspermia
  - Azoospermia → semen but with no sperms
  - Oligospermia → low count < 20 million / ml (may cause infertility)
  - Polyspermia → high count > 250 million / ml

- **Necrospermia** → all sperms dead } usually d.t. infections or
- **Asthenospermia** → weak sperms } immunological causes
- **Teratospermia** → excess abnormal forms > 85% (e.g. varicocele)
- **Pyospermia** → pus in semen (> 3–5 / HPF)

CASA (computer assisted semen analysis)

A....progressive forward motility................25%
B....sluggish motility.................OR A+B: 50%
C....abnormal motility
D....immotile

❖ Assessment of infertility

...... Male is assessed first ......

❶ HISTORY

▸ **Personal**

- Age-----------------testicular function declines gradually with age
- Marital status----If has children or not from previous marriage
- Address-----------rural areas (Bilhariziasis)
- Occupation-------. Exposure to heat (bakeries, ovens) → thermal injury
  . Exposure to irradiation or lead → testicular damage
- Special habits----Marijuana, smoking → impotence

▸ **C/O** ⇒ any *genital* or *urological* problems e.g. varicocele, urethral discharge

▸ **Past history**

- Surgical → hernia.......urinary / genital.......spine / CNS
- Medical → DM / TB / Mumps
- Drugs → . anti-hypertensive, antidepressant → impotence
  . cytotoxic, irradiation → germinal cell aplasia
  . anti-fungal, anti-malarial → ↓ spermatogenesis

❷ INVESTIGATIONS

▸ **Semen analysis**

Collected in a *sterile* container (& not condom)...after 3 days of abstinence

Normal semenogram

. **Macroscopic**

- Character------------viscid, whitish, liquefies within ½ hour
- Volume--------------2 to 4 ml
- Odor------------------characteristic
- pH--------------------alkaline (7.2 – 7.8)

. **Microscopic**

- Count------------------ > 20 ✓ million /ml (60–120 ☹)
- Morphology---------- > 30% have normal shape
- Motility--------------- > 50% show forward motility after 60 min
- Pus cells--------------less < 1– 2 /HPF
- Antisperm Abs ------- -ve (MAR) mixed agglut. reaction

▸ If azospermia ⇒ **testicular biopsy**

- If +ve → *obstructive* → vasography to know the site
- If –ve → *testicular* → 1. chromosome analysis
  2. FSH & LH (differentiates 1^{ry} / 2^{ry} test. failure)

▸ If OTA ⇒ **immunological studies or $C_{\&}S$**

Another way for Present History

- History suggestive of ovarian factor
  - Estrogen . Irregular menses
    . Lack of 2ry sexual ccc
    . Advanced age, hot flushes (POF)
  - Galactorrhea.....Headache, visual disturbances (pituitary adenoma)
  - Hirsutism
  - Changes in hair texture, weight, hot/cold intolerance (thyroid)
- History suggestive of tubal factor
  - Previous PID (fever, abdominal pain, discharge)
  - Previous surgery
  - Endometriosis (severe pain, bleeding)
- History suggestive of uterine factor
  - Hypomenorrhea (septic abortion, Ascherman)
  - Menorrhagia (endometrial polypi)
- History suggestive of cervical factor
  - Previous surgery to cervix
  - Excessive leucorrhea
  - Chronic backache

Then......assessment of ♀ female

▸ **Personal**

.Age---------------------. very young → ovulation not yet established
. older → have less chance, so proceed rapidly for ttt

.Marital status---------less chance on longer periods of infertility

.Parity-------------------to determine if 1^{ry} or 2^{ry} infertility

.Address-----------------Bilhariziasis: tubal block

.Occupation-------------irradiation or heavy metals → ovarian damage

.Special habits.....................................Personal History of the Husband

▸ **Complaint** ⇨ failure to conceive (1^{ry} or 2^{ry})
± amenorrhea ± galactorrhea ± hirsutism

▸ **Menstrual history**

Menarche---If delayed menarche or 1^{ry} amenorrhea → anovulatory disorders

D/C-----------. Irregularity → anovulation
. Dysmmenorrhea → - Spasmodic--------usually ovulatory
- Congestive--------pelvic pathology
- 2^{ry} spasmodic----endometriosis
. Premenstrual tension → usually ovulatory
. Premenstrual spotting → corpus luteum insufficiency

LMP--------important to plan treatment

▸ **Obstetric** (only in 2^{ry} infertility)

- Puerperal sepsis → Ascherman syndrome
- Severe hemorrhage → Sheehan syndrome

▸ **Past history**

- Medical → TB, DM, HTN, fever, endocrine disorders
- Surgical → CS, D&C, ovarian cystectomy, laparoscopy

▸ **Present history**

Amenorrhea------Galactorrhea----Hirsutism

Bleeding----------organic or functional (*ovular or anovular*)

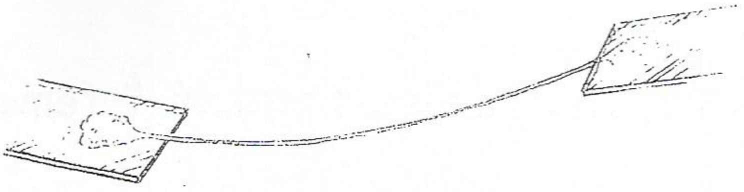
Discharge--------cervical or vaginal infection

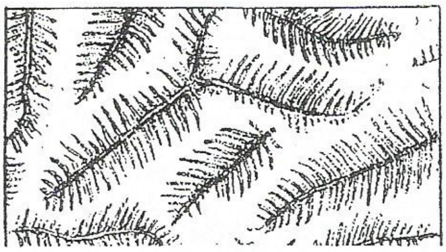
Enlargement ----abdominal swelling: fibroid or ovarian or pregnant

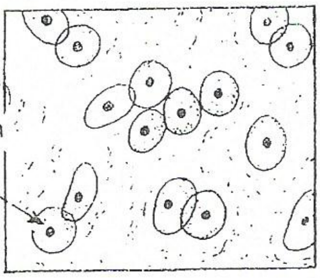
Pain----------------dyspareunia
. If superficial → vulvitis, vaginitis
. If deep → endometriosis, PID, tumors, displacement

Previous Infertility Investigations or Therapy Trials-------

▸ **Sexual history** ⇨ .... AS IN COITAL FACTORS



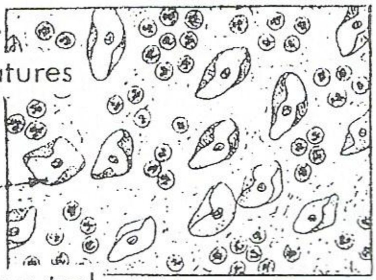




Pre-ovulatory squames.

A large cell with a small nucleus shows oestrogen stimulation

Post-ovulatory squames.



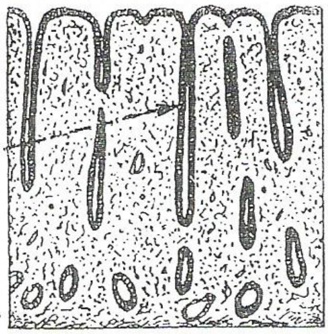
Progesterone matures the squames which develop rolled edges.

Note the 'shower of leucocytes'

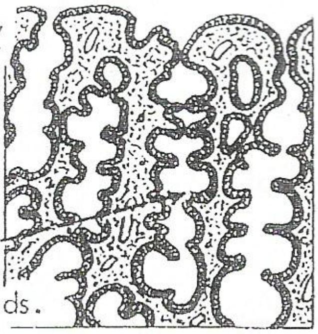
3. Endometrial Biopsy

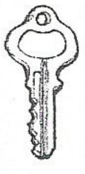
Premenstrual endometrium is clear evidence of an ovulatory cycle, but curettage or aspiration is uncomfortable for the patient, and not always feasible through a nulliparous cervix.

Pre-ovulatory endometrium showing oestrogen stimulation. Note the narrow non-secreting glands. The epithelial and stromal cells show proliferative activity.



Post-ovulatory endometrium showing the effect of progesterone. Note the dilated secretory glands.





There is no evidence that the use of temperature charts or LH "ovulation predictor" kits to time intercourse around ovulation mproves the chance of conception; body temperature is a poor predictor of ovulation, and LH kits, although better, are expensive. Also, timing intercourse is psychologically stressful and can be counterproductive.

A- Tests for Ovulation & CL function ✍

◈ Symptoms suggesting ovulation

- Regularity ✓✓ of cycles.....spasmodic dysmenorrhea....PMS
- Midcyclic (ovulatory) symptoms:-
    - *Discharge* → due to ↑ cervical secretion (E effect)
    - *Pain (Mittleschmertz)* → due to ovulation
    - *Spotting* → due to relative drop of estrogen level

◈ Tests for ovulation ΦΦ

- Morning BBT (0.2–0.3°c rise in 2nd half of cycle) d.t. 'P' ¤
    - **Biphasic** → ovulatory
    - **Monophasic** → anovular
    - **Short (10d)** → CL insufficiency

    Disadvantage: not so accurate, affected by infections & fevers

- Vaginal smear ⇨ progesterone effect (intermediate cells)

- Cervical mucous ⇨ profuse, +ve Spinnbarkeit, +ve fern....E effect
  turns –ve on day 17-21..................P effect

- Premenstrual endometrial biopsy ¤ (& disturb a possible pregnancy ??)
    - If ovulation → secretory endometrium
    - If CL insufficiency → lag behind menstrual dates by ≥ 2–3 days
    - Diagnosis of diseases of endometrium → TB endometritis

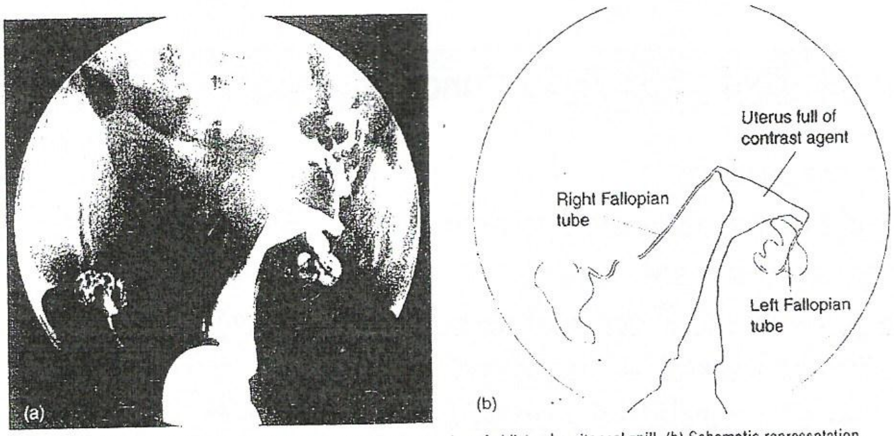
- Hormone assay
    - **Mid-luteal ✓ progesterone** (21¤)
        - >10 ng/ml → ovulation + good CL function
        - 5–10 ng/ml → ovulation + CL insufficiency
        - < 5 ng/ml → anovulation
    - **Urinary LH kits** ⇨ ovulation within 36 hrs (for early detection)

- Folliculometry (serial U/S) ⇨ gradual ↑ in follicle size to 20-22 mm
  followed by sudden collapse
  ⇨ tri-laminar endometrial lining

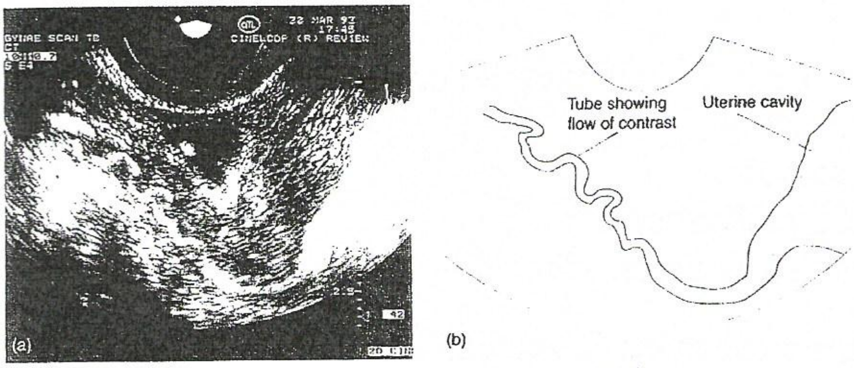
> **Ovarian reserve** is known by day 3 FSH, antral follicle count (TV-US), clomiphene challenge test, inhibin B and AMH (anti-Mullerian hormone)

◈ Tests for other ovulatory dysfunction

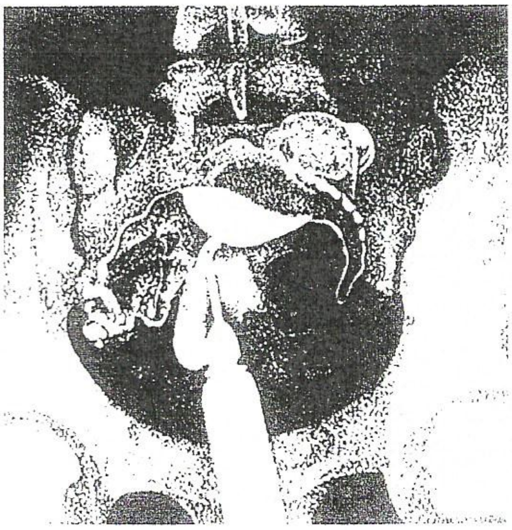
- If amenorrhea----------------Prolactin, $T_{3\,\&\,4}$, progesterone challenge test,
  Gn. assay...**day 3** ¤
- If hyperprolactinemia-----Prolactin, CT brain
- If hyperandrogenism------DHEA-S, testosterone

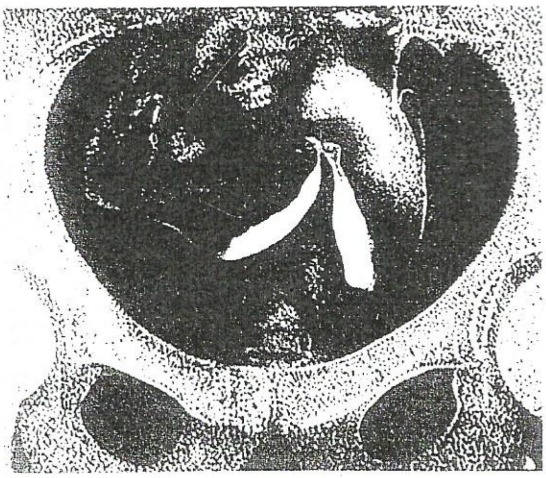


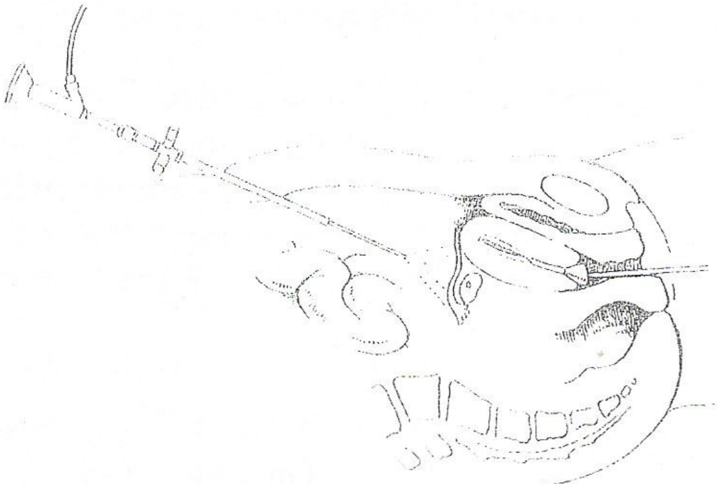
(a) Hysterosalpingogram confirming tubal patency; there is bilateral peritoneal spill. (b) Schematic representation.



(a) Hysterocontrast synography showing a Fallopian tube. (b) Schematic representation.







B- Tests for tubal patency

Indications ➡ infertility, after tubal surgery or myomectomy
Contraindications ➡ pregnancy, bleeding, infections
Timing ➡ **best is 2 – 3 days postmenstrual**
- To avoid disturbing a possible pregnancy
- Thin endometrium . ↓ risk of embolism or intravasation
  . ↓ risk of endometriosis
  . Avoid false negative results

① Hysterosalpingography

Method → radio-opaque material is injected through cx & x-ray is taken
Advantages
- *Diagnostic*......localizes exact site of pathology (uterus, tubes, peritoneum)
- *Therapeutic*...... .Pressure during injection can break some thin adhesions
  .I^2 has antibacterial effect

② Laparoscopy

	Diagnostic	Therapeutic
Tubes	Tubal block (to confirm HSG)	salpingolysis, salpingostomy
Ovary	PCO & other ovarian swellings	cautery for PCO, ovarian cystectomy
Endometriosis	Endometriotic petichiae & spots	cauterization of implants
Others	To evaluate unexplained infertility	Ovum pick up in IVF

③ HYstero-salpingo COntrast SonographY (HyCoSy)

- **Method** – Injection of Echovist (a galactose suspension) via the cx
  – The flow of solution is seen by transvaginal U/S
- **Advantage** ⇨ no radiation, no anesthesia, office procedure

④ Tuboscopy

- **Method** – *Falloposcopy→ trans-cx* endoscopy of tube (via hysteroscope)
  – *Salpingoscopy→ trans-abd.* endoscopy of tube (via laparoscope)
- **Advantage** ⇨ both tubal anatomy..&..**physiology** [mucosal cilia] are studied

⑤ Tubal cannulation

- **Method** – Transcervically, try to pass a catheter through the tubal ostium
  – This is done guided by hysteroscope
- **Advantage** ⇨ bypasses cornual block

⑥ Older methods ✗

- **Tubal Insufflation (Rubin's test)** – inject air through cx canal then do x-ray
- **Kymography** – pressure changes are recorded on a revolving drum

Role of Hysteroscopy in infertility

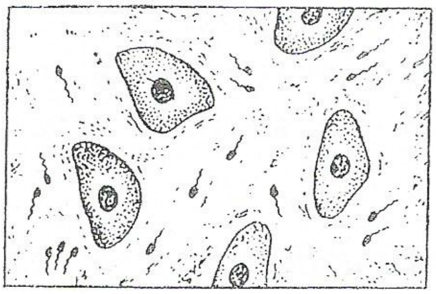
	Diagnostic	Therapeutic
Tubes	Tubal block (assess the cornu)	Cornual bypass (tubal cannula)
Uterus	Any major pathology - Fibroid - Septum - Ascherman	 - Polypectomy - Septo – metro– plasty - Adhesiolysis

Role of Ultrasonography in infertility

	Diagnostic	Therapeutic
Tubes	Saline sono- hysterography	Break thin adhesions
Ovary	Folliculometry	Ovum pick up in IVF
Uterus	Major pathology in ovary / uterus	U/S aspiration of ovarian cysts

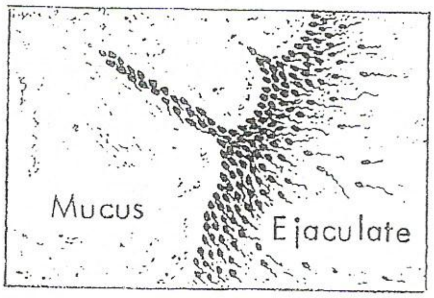
<u>The Postcoital Test</u> (PCT)

This test demonstrates the ability of sperm to remain motile in ovulatory cervical mucus. A sample of cervical mucus is obtained about 4 hours after coitus and examined microscopically. At least ten active sperms should be present in a high power field. Defects of motility are an indication for antibody testing.



<u>The Sperm Invasion Test</u> (SIT)

This test is carried out when the PCT is persistently negative, and requires a specimen of ejaculate, a drop of which is placed with a drop of cervical mucus on a warmed slide. The sperms should be observed actively invading the mucus.



C- Tests for uterine factor

- Ultrasonography (Q..What is the value of U/S in infertility?)
- Hysteroscopy (Q..What is the value of hysteroscopy in infertility?)
- Premenstrual endometrial biopsy
- Hysterosalpingography

D- Tests for Cx & vagina

- Sims-Huhner postcoital test
  - Semen analysis must be normal
  - Intercourse is done at midcycle ¤ (favorable cx mucus) after abstinence 3 days
  - 6 hrs later, a drop of cx mucous is collected
  - Normally → sperms are found to have forward motility in the cx mucous
  - The following is assessed (Moghissi score)

1] **Cervical mucus score** (0,1,2,3) for

. Amount......viscosity.....Spinnbarkeit....Ferning....cellularity

. Total score <5 → HOSTILE cx mucus

5-10 → UNFAVORABLE cx mucus

10-15 → FAVORABLE cx mucus

2] **Sperm count & motility assessment**

. More than 5-20 / HPF sperms with forward motility / HPF

. Immotile, shaking, rotatory movement denotes *infection / antibodies*

**** Etiology of cx hostility or –ve PCT ****

- **Wrong time of cycle** → Pr. effect or lack of adequate estrogen effect
- **Poor glandular secretion d.t.**
  - Congenital, poor estrogen response, CLOMID therapy
  - Destruction of glands by cautery or amputation
- **Infection** → $C_{\&}S$ from vaginal & cervical mucus
- **Immunological factors** → cervical mucus (IgG) or in serum (IgM)
- ... **Coital factors** → dyspareunia, impotence, premature ejaculation

- Sperm penetration test (Done if PCT is -ve) = cx mucous contact test

1] **Slide test**

. Cx mucus + donor healthy semen → detect abnormality in mucus

. Donor healthy cx mucus + semen → detect abnormality in sperms

2] **Capillary tube test**

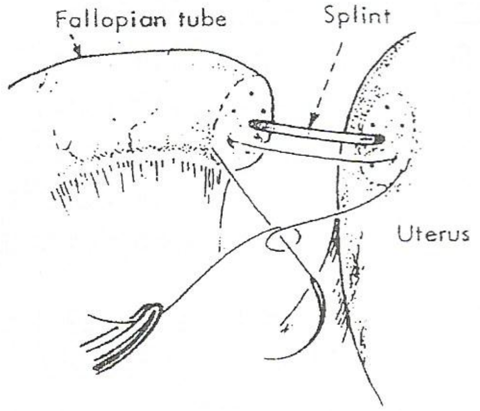
. Semen is put in a reservoir & cx mucus is sucked in a cap. tube

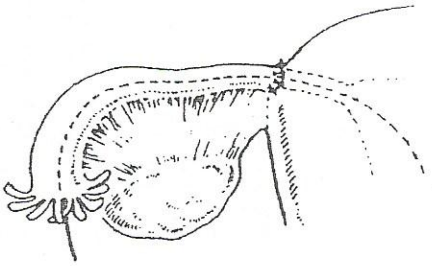
. The tube is examined for sperm migration after 30, 60, 180 min

Factors adversely affecting conception rates		
Female factors	Male factors	Combined factors
Age (>37 years)	Low numbers of motile, healthy sperm	Duration of infertility (>2 years)
Menstrual FSH level (>10 u/L)	Drug intake	No previous conception in current relationship

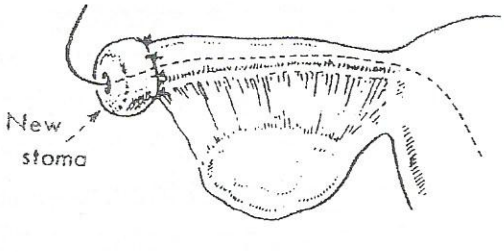
FSH, follicle-stimulating hormone.

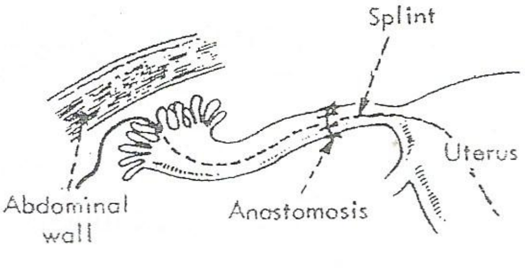
Preconception advice	
Lifestyle	Medical
Stop smoking	Optimize management of medical problems
Stop recreational drugs	Eliminate drugs not safe for pregnancy
	Optimize body weight to a body mass index of 20–30
	Eliminate drugs not safe for pregnancy
Regular sexual intercourse, 2–3 times a week	Prepregnancy assessment by an obstetric physician
	Commence folic acid supplements
	Ensure immunity to rubella





The tube is guided into the uterus and sutured in place.





Treatment of female infertility →

▸ **general** ....PCR-GG............

- Correct PSYCHOLOGICAL factors
- Correct COITAL errors….good timing
- REASSURANCE if the patient seeks rapid outcome
- Improve GENERAL health
- Treatment of any GROSS pathology (fibroid) or local infections

▸ **if ovarian cause**

- Anovulation e.g. PCO → induction of ovulation….lap. ov drilling
- Hyperprolactinemia → dopaminergic drugs
- LUFS → induction of ovulation
- LPD → prog. in the 2nd ½ of the cycle
- Resistant ovary syndrome → induction by high doses Gn.

▸ **if peritoneal cause** (*endometriosis*)

- Induction of ovulation → if no masses or adhesions found
- Surgery if there are → masses or tuboplasty if → tubal adhesions

▸ **if tubal cause** .... *tuboplasty (microsurgery)*...........

Peritubal adhesiolysis (lysis of adhesions) → best prognosis ✓
Neosalpingostomy → new opening (as in hydrosalpinx)
End to end anastomosis → to bypass occluded segment
Tubal reimplantation → in isthmic block ✗

- *Laparoscopy* is better than laparotomy
- *Previously* repeated *tubal insufflation or* hydrotubation were tried
- *Prognosis* is *poor* (conception rate 10–40%, ectopic may occur)

▸ **if uterine cause** ⇨ *surgery* e.g. polypectomy, myomectomy, hysteroscopic lysis of adhesions in Ascherman syndrome, metroplasty

......**What is surrogate mother?**

▸ **if cervical causes**

- Cervical infection → antibiotic according to C&S or cauterization
- Poor quality of cx mucus → CEE (Premarin) 0.625 mg at days 10,11,12
- Immune causes → steroids ± condom for 6 months → to ↓ antibody level
- Failure / resistant cases ➡ **AIH**

▸ **in all cases**......if failed......➡ **ART**

Ovulation Induction:

❶ Antiestrogens

- **Clomiphene citrate** (Clomid) → 50 mg
- **Tamoxifen** (Nolvadex) → 10 mg /12 hrs
- **Aromatase inhibitors** (Letrozole)

..............Clomid ....

Action

. Synthetic non-steroidal antiestrogen ¤

. Competes with E for its receptors on pit. & hypoth. (hypo-estrogenemia)

→ Decreased –ve feedback on FSH & GnRH

→ ↑ GnRH → ↑ FSH & LH → follicular development

Dose (Tab = 50 mg ¤)

. 1 x 2 x 5 starting from the 2nd (5th) day of the cycle for 6 cycles

. If there is amenorrhea → give progesterone…withdrawal bleeding...then start

. If no ovulation → increase the dose up to 5 tab /day (250 mg)

Side effects ¤

. Hot flushes, dry vagina, breast tenderness, headache, visual disturbance

. Multiple pregnancy (5-10%)

. OHSS (**O**varian **H**yper **S**timulation **S**yndrome) → rare

. Relation to tumors….→ NOT proved to ⇧ cancer ovary

↘ MAY → endomet cr after 5 yrs (loses its antagonistic action)

Results

↘ **Good response** (75%) **known by**

- Biphasic Body Temperature
- Mid-luteal progesterone
- U/S → folliculometry (mature Graafian follicle = 18-22 mm)

↘ **No response (CC failure or resistance) m.b.d.t.**

- Another cause of infertility
- Poor cx mucous ¤ (anti-E effect) → add small dose of E_2 at ovulation
- LPD → give HCG or progesterone
- LUF → give HCG

↘ **If failed, may add the following**

- Metformin → <u>ONLY</u> in cases with <u>PROVEN</u> insulin resistance in PCO
- Bromocriptine → even if the prolactin level is normal
- Thyroxin → in cases of hypothyroidism
- Dexamethasone → suppress adrenal androgen
- Nalotrexone (opioid receptor blocker) → opiods ↓ GnRH release

② Antiestrogen + HCG

- **Preparation**
  - *Pregnant urine* → Pregnyl, Profasi (IM)
  - *Recombinant DNA* → Ovidrel (SC)
- **Action**.................. acts like LH
- **Dose** ⇒ 5.000 – 10.000 IU given IM when:-
  - The leading GF is mature (18-20 mm)
  - E_2 is 1000-1500 pg/ml (not given if > 2000 to avoid OHSS)

  ⇒ advice intercourse on same & next day of injection

③ Human Menopausal Gn (HMG)

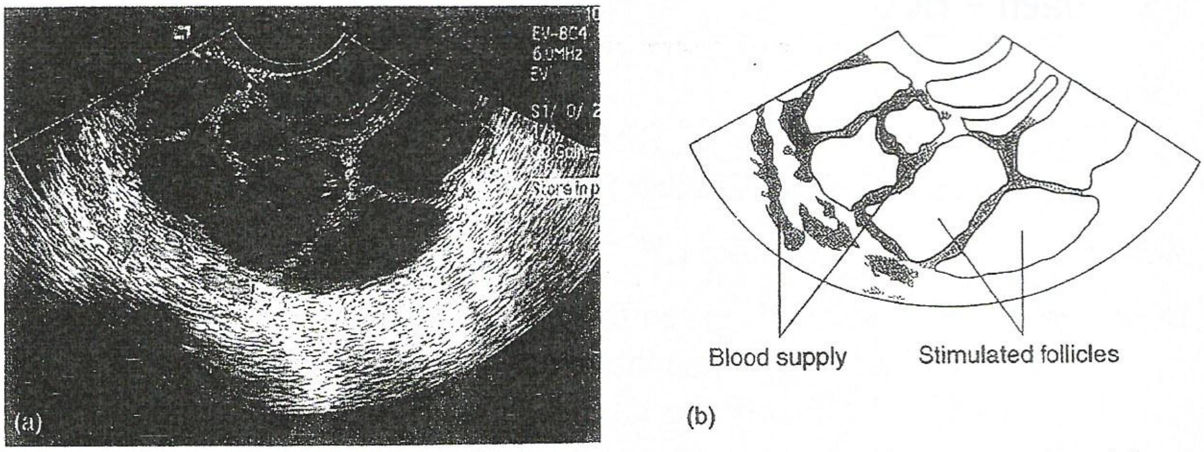
- **Preparation**
  - *Postmenopausal urine* (IM)
    - Both FSH (150 IU) & LH (**75 IU**) → Pergonal, Humegon
    - Mainly FSH (150 IU) & LH (**< 1 IU**) → Metrodin (esp for PCO)
  - *DNA* (SC) : FSH ...... & LH (**no**) → Puregon, Gonal F
- **Dose** ⇒ 1–2 ampoules on 3rd day of cycle → repeated on days 5, 7, 9
  - HCG is given according to folliculometry & serum E_2
  - Combination with AIH may improve outcome
- **Response**
  - Ovulation occurs in more than > 90% per treatment cycle
  - Treatment is continued for 3-4 successive cycles
- **Side effects**
  1. Multiple pregnancy.........20% ¤
  2. Abortion & PTL............15%
  3. Ectopic pregnancy...........5%
  4. OHSS.........................2%

> **Other indications of HMG**
> - Hypothalamic-pituitary failure (group I & II) ¤
> - Unexplained infertility
> - To induce superovulation for ART procedures

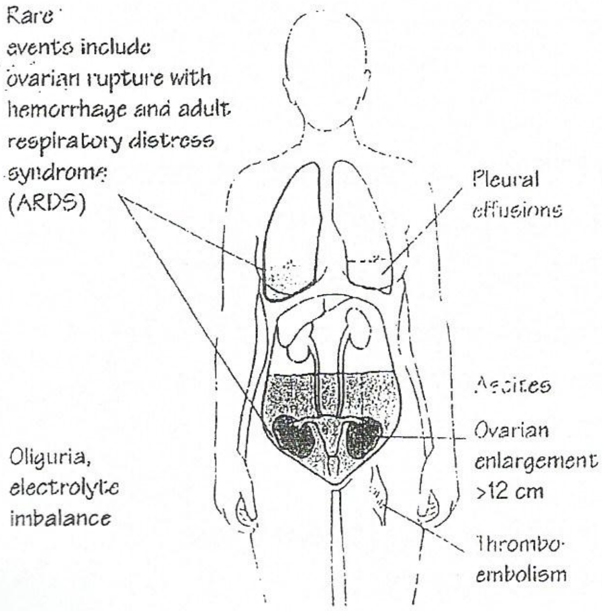
④ GnRH (LHrH)

- **Dose** ⇒ every 60 – 90 min for 2–4 wks by:

  ↘ a special pump (IV or SC)....OR.....nasal spray ✔
- **Adv** ⇒ used if ovary is resistant to induction
- **Disadv** ⇒ expensive & difficult



(a) Ultrasound showing stimulated ovary with multiple follicles and associated blood supply. (b) Schematic representation.



Ovarian Hyperstimulation Syndrome (OHSS)

Pathogenesis

- HCG injection → ↑ PG.....E_2......histamine → ↑ capillary permeability
  → shift of fluid from *intravascular* to *extravascular* space
- It occurs ONLY after injection of HCG (3-6 days after injection)
  ↘ RARE with clomid alone
  ↘ NEVER with GnRH ¤
- Prognosis will be worsened if .... test is +ve (why ?)

Clinical picture

1. **Mild form** → ovarian enlargement *without* cyst formation
   + abdominal discomfort

2. **Moderate form** → ovarian enlargement *with* cysts < 10 cm
   + abdominal pain, $N_{\&}V$, diarrhea and weight gain

3. **Severe form** ¤ → as above but cysts are large
   + . hypovolaemia, hypotension, oliguria
   . haemoconcentration → DVT & embolism
   . ↓ renal perfusion → Na & H_2O retention → edema, ascites, pleural effusion, hyperkalemia & acidosis

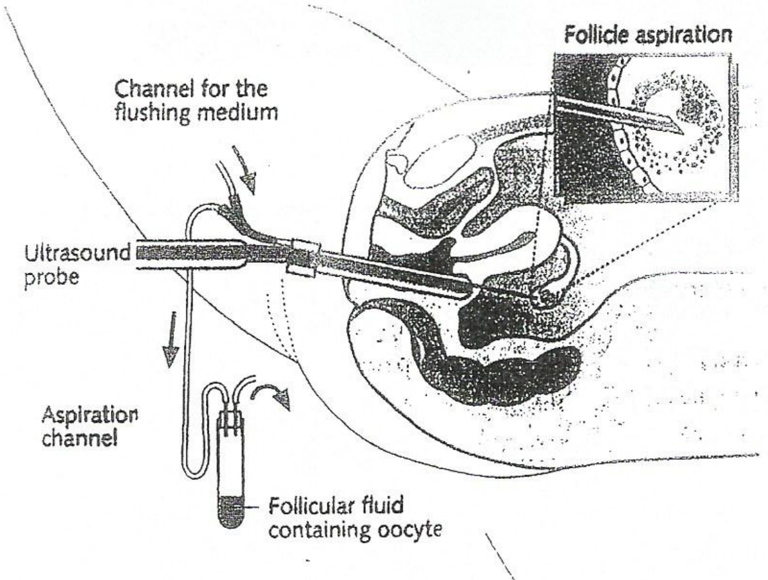
Treatment

- **Prophylaxis** ⟹ avoid HCG injection if - serum E_2 is > 2000 pg/ml
  - ≥ 3 follicles each ≥ 16 mm
- **Mild form** ⟹ no treatment (rest at home + frequent follow-up)
- **Moderate & severe** ⟹ HOSPITALIZATION (even in ICU) +
  1. Complete bed rest + no P/V (to avoid ovarian rupture)
  2. Analgesics for pain, anti-histaminics, anti-prostaglandins

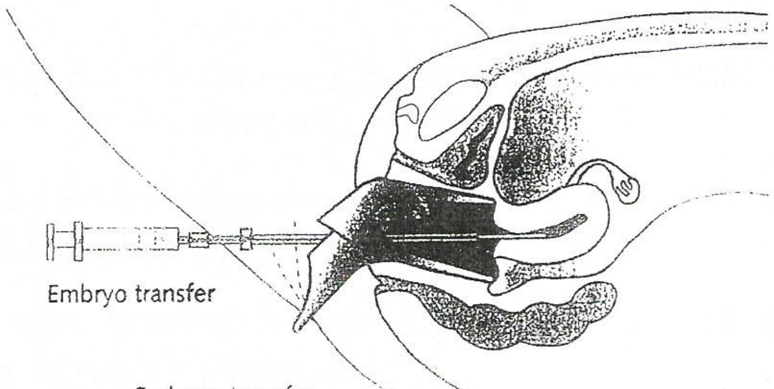
  ⇨ **Fluid & salt restriction to reduce ascites, hydrothorax**
  - No diuretics (↑ hypovolaemia → ↑ haemoconcentration)
  - Fluid chart to monitor intake & output
  - Paracentesis or pleurocentesis (in resistant cases) ¤

  ⇨ **Follow up of**
  - Vital data (P, T, BPr)
  - Hct, BUN, creatinine, coagulation profile, ECG (↑ K)
  - U/S to follow the decrease in size of ovaries

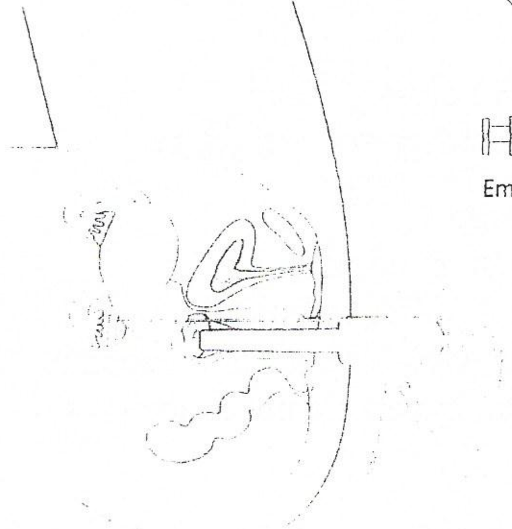
  5. No laparotomy EXCEPT IF ¤ → complicated cysts (rupture, torsion)
  6. New lines of therapy: Heparin / Albumin



Egg collection.



Embryo transfer.



Assisted Reproductive Technology (ART)

❶ In Vitro Fertilization & Embryo Transfer –IVF & ET–

▸ **Indications**

- Tubes → damaged or absent
- Peritoneum → dense adhesions e.g. endometriosis
- Hostile α (e.g. antibodies or infections) → after failed IUI
- Unexplained infertility ¤
- Male infertility → d.t. severe OTA (only few thousands are needed)

▸ **Technique**

1. *Superovulation* ➡ multiple ova
   - Down-regulation by GnRH ¤ (inhibits ovarian function < induction)
     - * Long protocol......starts day 21 of the previous cycle
     - * Short protocol (flare up)....starts with the same cycle
   - Then give: different protocols of HMG → folliculometry follow up
   - Then give: HCG IM → complete ovum maturation within 34-36 hr ¤
2. *Oocyte(pick-up) retrieval* ➡ transvaginal U/S ✓
3. *Fertilization in vitro*

   - Ova are incubated in a culture medium at 37°c for 4-6 hours
   - Then prepared sperms are added for fertilization.
   - Wait till the fertilized egg reaches 4–8 cell stage (takes 48 hrs)
4. *Embryo transfer*
   - The fertilized eggs are injected into the uterine cavity near fundus
   - Transfer (acc. to age) 2-3 embryos to ↓ % of multiple pregnancy
   - The remaining embryos are frozen (cryo-preservation) for later use
5. *Luteal phase support* ➡ progesterone or HCG

▸ **Results**

- The procedure is repeated for 3 or 4 successive cycles
- The pregnancy rate is 20-30 % (25 yrs) – 10% (40 yrs) per ttt cycle
- Multiple pregnancy occurs in about 35%
- Ectopic pregnancy occurs in about 3 %

❷ Gamete Intrafallopian Transfer –GIFT–

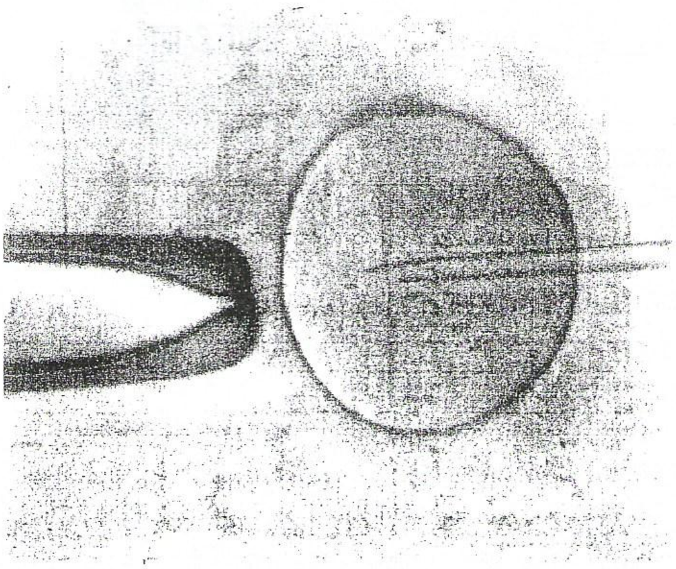
▸ **Oocyte & sperms** are placed into the fallopian tubes either through:

ς *Ampulla* (via laparoscope) or *Isthmus* (via hysteroscope)

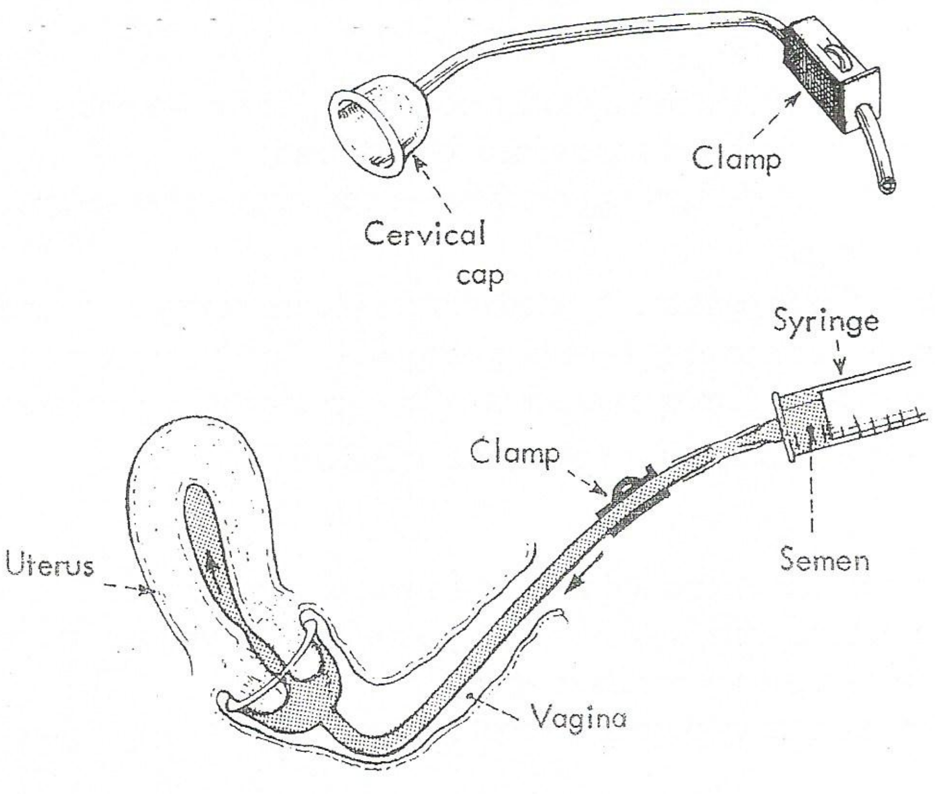
▸ **Results** ➡ 30% preg. rate (better than IVF but with > ectopic)

❸ Zygote Intrafallopian Transfer –ZIFT–

▸ The fertilized oocytes are placed into the tubes as **zygotes**



Intracytoplasmic sperm injection.



Micro-insemination

▸ **Intracytoplasmic sperm injection –ICSI– ✓**

* **Technique**

- A single sperm is injected into the cytoplasm under microscope
- In case of obstructive azoospermia, sperms are aspirated by:
  - **MESA** (microinsemination after epididymal sperm aspiration)
  - **TESA** (testicular sperm aspiration)

* **Indications**

- Failure of IVF trials (better results)
- Refractory unexplained infertility
- Marked *oligospermia*
- Marked *asthenospermia*

▸ **Subzonal insemination –SUZI– ✗**

* **Technique**

- A hole is made in the zona pellucida (enzymatic, laser, zona drill)
- 3-6 spermatozoa are introduced into the subzonal space

* **Results** → fertilization rate is 15-30% (∴ replaced by ICSI = 30–60%)

Artificial insemination

▸ **Indications**

* **Artificial insemination husband (AIH)**

- Coital factor (failure of deposition of semen in the vagina)
- Male infertility (OTA)
- Cervical hostility
- Unexplained infertility

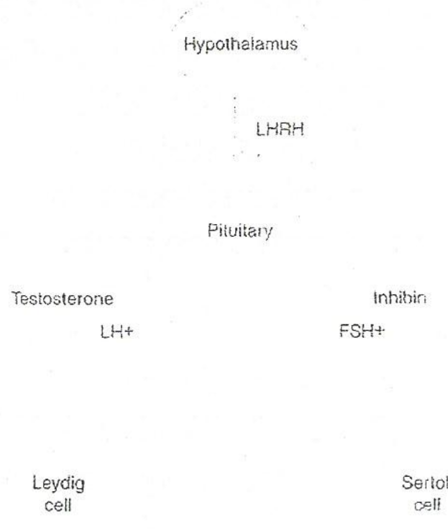
* **Artificial insemination donor** → in sterile husband (unreligious, unethical)

▸ **Technique**

1. *Induction of ovulation*
   - Better results when AIH is done with induction of ovulation
   - Better results with gonadotrophins than clomid
2. *Processing (preparation) of semen*
   - Anti-PG.....................as it → uterine cramps (expulsion of sperms)
   - Anti-biotic.............. if pyospermia
   - Proteolytic...............↓ viscosity
   - Caffeine, Kallikerine.....asthenospermia
3. *Injection* of 0.3 – 0.8 ml intrauterine (IUI) by special catheter

History

The technique was pioneered in the 1970s by Patrick Steptoe and Professor Robert Edwards, initially in Oldham and then at Bourn Hall, Cambridge. The first pregnancy, an ectopic, was established in 1976, but it was not until 1978 that the first baby, Louise Brown, was born. Although this success was based on the single oocyte developed during a normal ovulatory cycle, it soon became clear that a higher pregnancy rate could be achieved if a greater number of oocytes were obtained by superovulation.



Flow diagram illustrating the relationships of the hypothalamo–pituitary–testicular axis. (LH, luteinizing hormone; FSH, follicle-stimulating hormone; LHRH, luteinizing hormone-releasing hormone.)

-- Extras --

History

- **Louise Brown** (1^{st} IVF born child) 1978 has gone her own baby naturally
- **Edwards & Steptoe** (British) won Noble prize (2010) for developing IVF

Advanced facts in ART

- **Ovarian reserve** (to assess how much ova are present to predict IVF success) is known by ❶ *ovarian volume, antral follicle count,* ❶*FSH, LH, E_2 level, inhibin B,* AMH (***anti-Mullerian hormone***) ❸ *Doppler*
- **Superovulation** doesn't lead to early menopause
- **Number of follicles** doesn't guarantee number of eggs to be collected
- **Embryo grading** (1✓-2-3-4×) depends on ❶Rapid division, ❷equality of cells, ❸fragmentation
- **Number of embryo transfer** depends mainly on *age* (max 3). Recently there is a strong drive for SET (*single embryo transfer*)
- **Selective embryo reduction** is better to be performed If triplets results
- **Cryo-preservation:** Sperm freezing is best – Embryo freezing is more successful > egg freezing – Ov. tissue freezing is still experimental
- **Sex determination** is possible by PGD (*pre-implantation genetic diagnosis*)
- **Assisted laser hatching** (to zona pellucida) may improve embryo uptake. Still the most difficult step to be controlled is embryo uptake by endomet.
- **CFMF** < 1 % (e.g. hypospadius) is not more than in natural cycles
- **Blastocyst transfer** (*day*❺) is recently popular than ET (*day*❷). The embryo that divides till blastocyst stage is probably healthier with better success

Management of male infertility

- Chronic prostatitis → antibiotics (according to C&S) for long time
- Persistent low sperm count
  - Clomiphene 25 mg /d for 25 days + mucolytic
  - Gonadotrophins (if FSH is low)
- Hyperprolactinemia → bromocryptine
- Varicocele → surgery (improves quality if it is significant – grade III)
- Impotence, premature ejaculation → IUI (AID)
- Oligospermia → ICSI
- Obstruction → TESA, MESA

Causes of sterility

- Female → POF.....absent ovaries (Turner).......uterus (M. agenesis)
- Male → Klinefelter syndrome....................absent testis (Mumps)

Chapter 4

Contraception

Physiological

Mechanical

IUCD

Hormonal contraception

Surgical sterilization

Ranking of contraceptive methods by rate of effectiveness

		Failure rates per 100HWY
Group A	**Most effective**	
	Tubal ligation/vasectomy	0.005–0.04
	Combined oral	0.005–0.30
	Sequential oral	0.20–0.56
Group B	**Highly effective**	
	IUD	0.5–3.5
	Continuous progestogen	1.5–2.3
	Diaphragm or condom and cream	
	All users	4.0–7.0
	Highly motivated	1.5–3.0
	Periodic abstinence	
	All users	10.0–30.0
	Highly motivated	2.5–5.0
Group C	**Less effective**	
	Coitus interruptus	30.0–40.0
	Vaginal foam or cream	30.0–40.0
Group D	**Least effective**	
	Postcoital douche	45.0
	Prolonged breastfeeding	45.0

Family planning

Jobs of family planning

- *Pregnancy spacing* (whether reversible or permanent)
- Management of *infertility*
- Management of *recurrent fetal loss & genetic counseling*

Methods used

Physiological	Mechanical	Chemical	IUCD	Hormonal	Surgical
Safe period - Calendar - Basal body temp - Cervical mucus Prolonged lactation Coitus interruptus Coitus interfemoris	Male condom Female condom Vag. diaphragm Cervical cap Vag. sponge	Spermicidal Foam Effervescent Tablets Cream Suppositorie s Jelly C-film	Inert Medicated - Copper - Progest. (mirena)	OCP 1. COC 2. POP Injectable Norplant Vaginal rings Hormone IUD	Female -Laparoscopy -Laparotomy -Hysteroscopy Male Vasectomy

"No ideal contraception is present; we use only the most suitable"

Q. what are the contraindications for pregnancy ?? see last page

They could be divided into

- **Hormonal**
  - Combined (E + P) ⟹ OCP.....monthly injectable........vaginal ring........skin patch
  - Progesterone only ⟹ POP..... injectable (DMPA)....implants....Pr. releasing IUCD
- **Non-hormonal** ⟹ 1.physiological, 2.barrier, 3.chemical, 4.IUCD, 5.surgical

----

- **Short acting**..........physiological, barrier, chemical, OCPs
- **Long acting**...........implants, injectables, IUCD, surgical

----

- **Irreversible** ⟹ surgical
- **Reversible** ⟹ all others

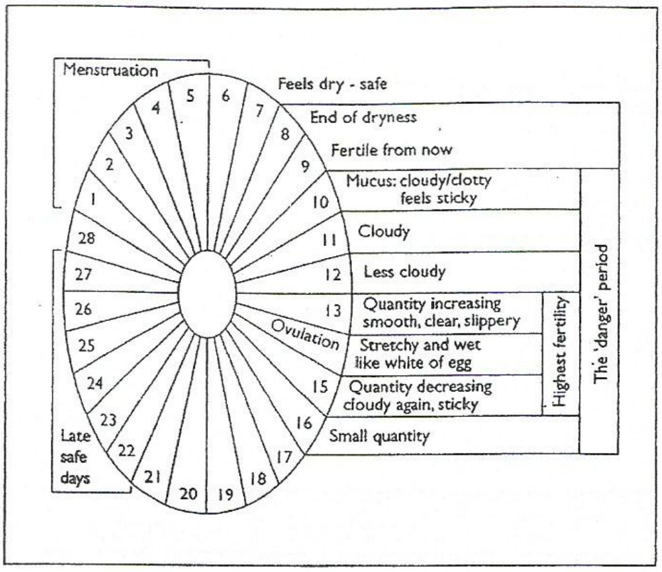
Pearl index (PI)

It is method used to determine the pregnancy (FAILURE) rate
- *among* 100 women (HWY)
- *using* a contraceptive method for 12 months

* *Perfect* use *rate* → represents the theoretical efficiency

* *Typical* use *rate* → represents the actual users' experience

.........Highly effective method has a failure rate < 1/HWY.........

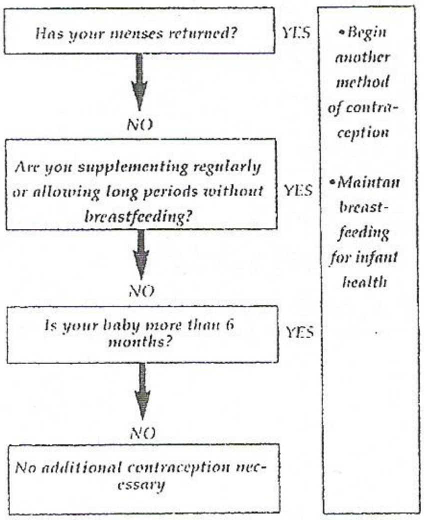


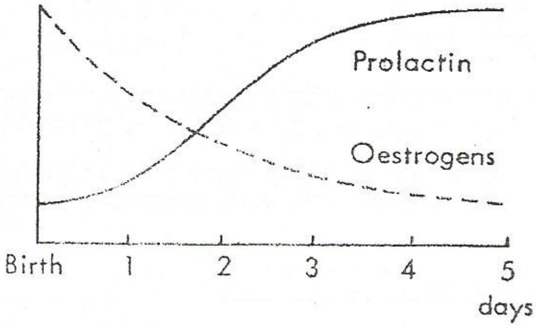
Periodic abstinence: the mucus (ovulation) method.

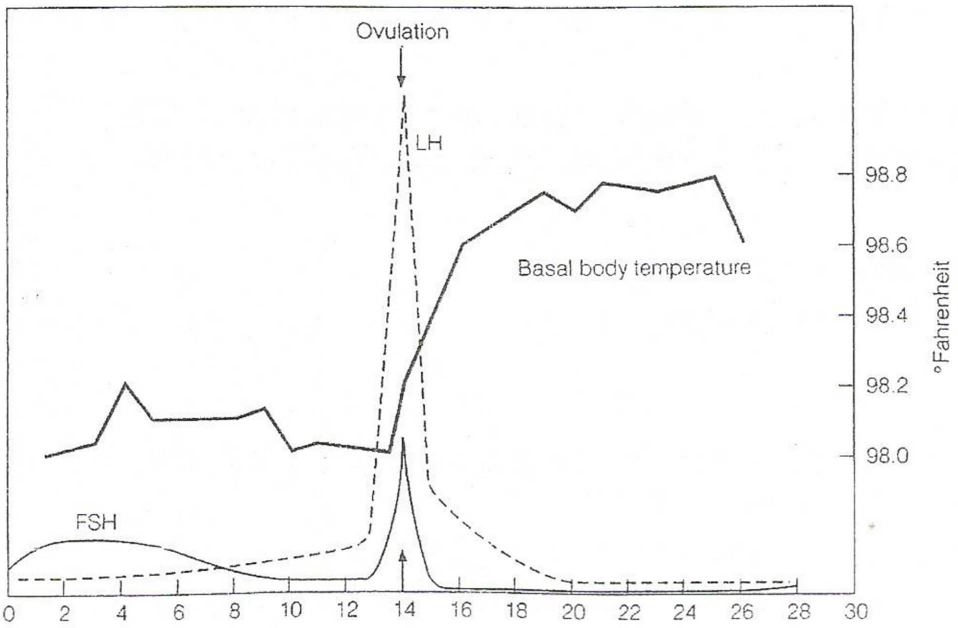
KEY POINTS

1. Natural family planning methods are the least effective methods of contraception and should not be used if pregnancy prevention is a high priority.
2. These methods rely on physiology to prevent pregnancy and require highly motivated users.
3. Periodic abstinence relies on accurate prediction of ovulation and abstinence from intercourse during periods of maximal fertility.
4. Coitus interruptus has a high failure rate attributed to the need for sufficient self-control to withdraw the penis before ejaculation and the high likelihood of deposition of pre-ejaculate into the vagina.
5. The length of lactational amenorrhea varies widely during breast-feeding; therefore, breast-feeding should be used for contraception for a maximum of 6 months after delivery.

Using the LAM Algorithm







1) PHYSIOLOGICAL

❶ Safe period: -fertility awareness-

* Calendar method ⇨ ovulation occurs 14 d < the 1st day of the next cycle
  . I.C. is avoided 2 days < & 2 days > the calculated day
  . Ovum lives → 24 hrs / sperms live 48 hours

* Basal body temperature ⇨ I.C. is only allowed after ovulation has occurred by 3 d, i.e. after 3 d of rise of BBT

* Cervical mucus method ⇨ I.C. is allowed only after 3 days from disappearance of wetness
  'Billing's method'
  - Estrogen → profuse α mucous → wet sensation
  - After ovulation, CL → progesterone → dryness of secretion
  - The BEST is *combination* (sympto-thermal) ¤

* Urinary LH kits (Persona) ⇨ detects ovulation by LH surge in urine

Requirement ▶	regular cycles, educated & motivated couples
Advantage ▶	no medical contraindications
Disadvantage ▶	limitation of IC + high failure rate (15–30 / HWY)

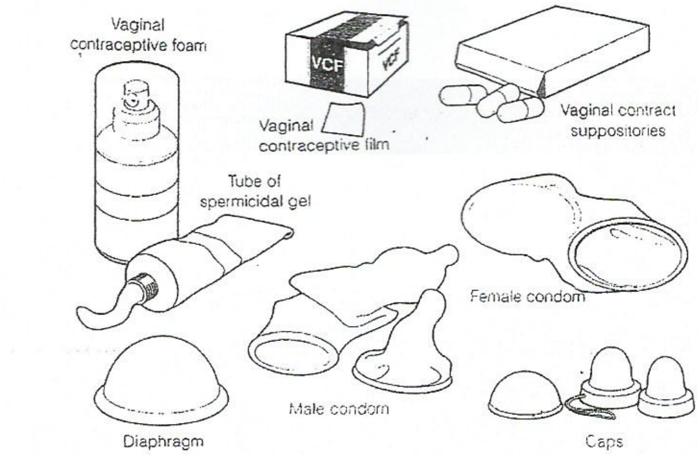
❷ Lactational amenorrhea method

Idea: prolactin → inhibition of ovulation
Increasing efficiency (from 10 → 90 %) **if:** ¤
- Amenorrhea is still present
- Regular breast feeding (6 by day & 2 by night)
- No supplementary food is given

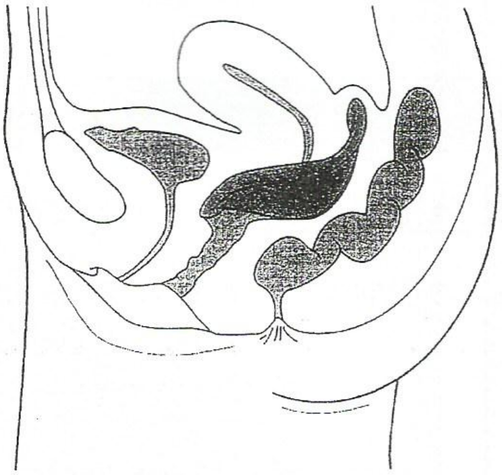
Advantage → available from 1st day, not costy, healthy to infant
Disadvantage
- Not so reliable (esp if breakthrough bleeding occur) ¤
- Effective mainly in the 1st 6 months ¤

❸ Coitus interruptus & interfemoris

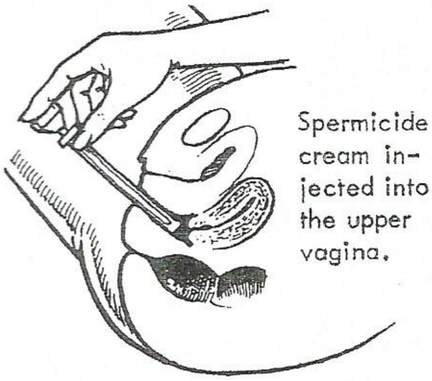
Idea → withdrawal of penis and ejaculation outside the vagina or intercourse between both thighs
Disadvantages
- Pregnancy may occur in spite of ejaculation outside the vagina as the pre-ejaculatory fluid may contain sperms
- Less sexual satisfaction → pelvic congestion
  ç menorrhagia, leucorrhea & backache

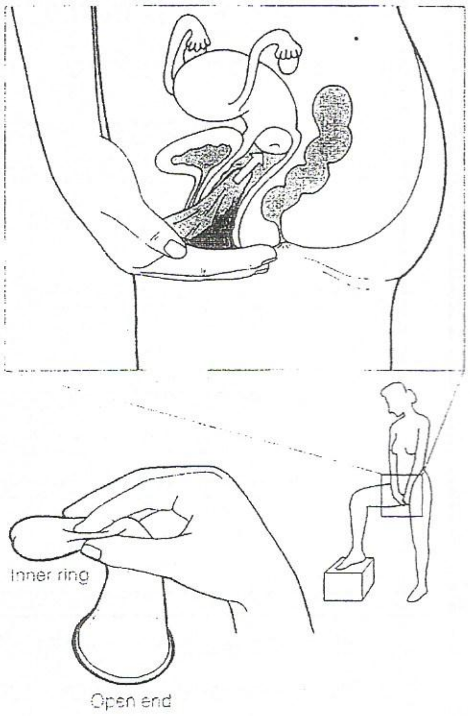


• Barrier methods and spermicides.

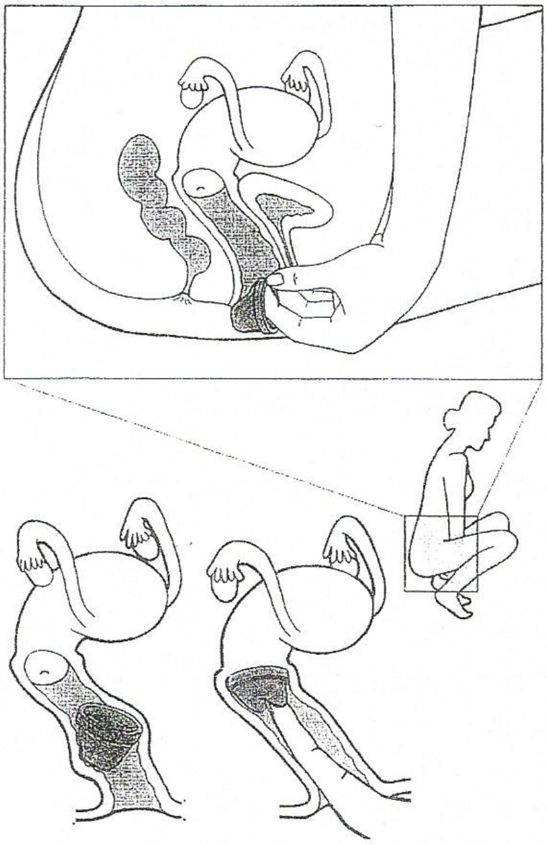


• Placement of the vaginal diaphragm.





• Placement of the female condom.



• Placement of the cervical cap.

KEY POINTS

1. Condoms, diaphragms, and cervical caps act as mechanical barriers between sperm and egg. Their efficacy is rate is 80% to 90% with practical use.
2. Condoms and spermicides containing nonoxynol-9 provide prophylaxis against STDs.
3. Diaphragms and cervical caps must be prescribed and fitted by a physician.
4. Spermicides come in a variety of over-the-counter forms at minimal cost. Spermicides have both a barrier and spermicidal effect.
5. Efficacy of spermicides is 75% to 80%, but variability in user technique can significantly lower efficacy.
6. Efficacy rates are greatly improved when using both barrier and spermicidal methods together.

2) MECHANICAL

1] **Condom** **(French Letter)** 15 x 3.5 x 0.02–0.07

- No side effects or contraindications
- Non contraceptive benefits →
  - Protect against STD ¤ , PID, CIN
  - Treatment of immunological infertility
  - Collection of semen for semen analysis (spermicide free)

2] **Female condom** **(vaginal pouch)**
- A polyethylene rubber sheath which lines the vagina (17 x 8 cm)
- Has 2 ends ⇔ a closed end and an open end

3] **Vaginal diaphragm** **(Dutch cap)** 50–95 mm
- Inserted in vagina < IC & removed after 8 hrs (till all sperms die)
- Disadvantages
  - Difficult to apply → needs well training in the clinic ¤
  - May lead to cystitis if large size, not suitable in prolapse

4] **Cervical cap**
- Applied directly to cervix (22–25–28–31 mm)
- Used if there is prolapse (diaphragm can't be applied)

5] **Vaginal sponge** **(Today)**
- Synthetic polyurethane sponge containing Nonoxynol-9
- Very easy to insert & remove (up to 24 hours)
- Disadv. → Toxic shock syndrome if left long (staph aureus ¤)

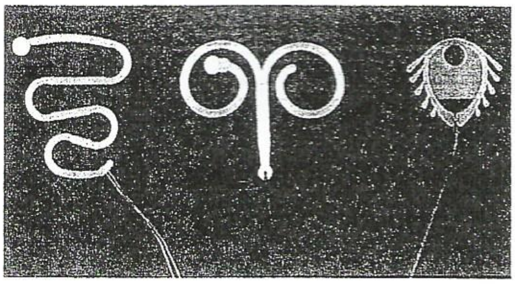
Advantages	Disadvantages
No effect on fertility/ lactation	Failure rate → 3–14 / HWY (improved by adding spermicidals)
No systemic side effects	May lead to allergic reaction (latex)
Easy to initiate & continue	Interrupt natural act (↓ sensation + ↑ erectile difficulties
Condom protect against STD	Sponge → infection.......Diaphragm → discomfort

3) CHEMICAL

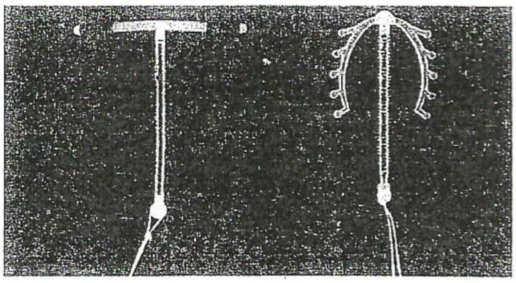
* **Method**
- Spermicidals → **Nonoxynol-9** & **Octoxynol-9**
- Action → destroy sperm memb + ↓ O_2 uptake

* **Supplied as** foam / jell / cream / effervescent tablets / suppositories

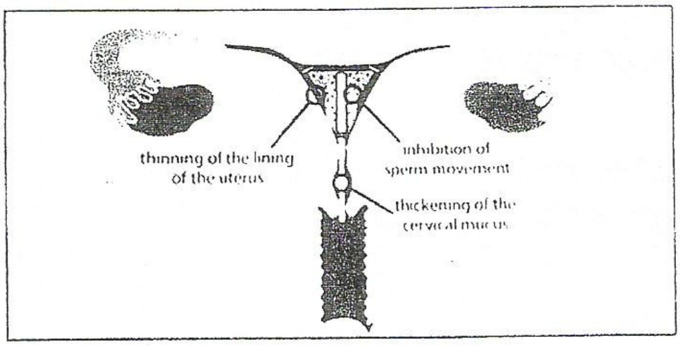
* **Use** ⇔
- Inserted 15 min before intercourse } high failure rate
- Intercourse must occur within 2 hours } =
- Delay postcoital douching for 6 hours } 30 / HWY

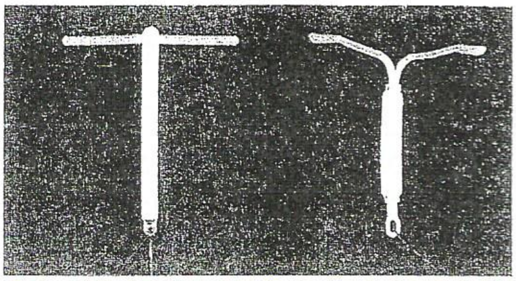


Plastic intrauterine devices: Lippes Loop, Saf-T coil, Dalkon shield.



Copper-bearing intrauterine devices: Multiload, Copper T 380.





Hormone-releasing intrauterine devices: progesterone-releasing IUD, levonorgestrel-releasing IUD.

Levonorgestrel-releasing intrauterine system

Advantages	Disadvantages
Highly effective	Persistent spotting and irregular bleeding in first few months of use
Dramatic reduction in menstrual blood loss	Progestogenic side effects, e.g. acne, breast tenderness
Protection against pelvic inflammatory disease	

4] INTRAUTERINE DEVICE (IUCD)

Made of . Polyethylene (non-irritant plastic), with 2 nylon threads
↘ marker for its presence & facilitates removal
. Barium → make them radio-opaque to confirm their site

Types

	Types	Duration
1] **Inert** Replaced now by medicated devices	**Lippes loop:** Double S shaped 4 sizes:- ABCD	Indefinite
2] **Medicated** Most commonly used now are→ -less pain & bleeding -better pregn. protecti	**With copper** - Cu 7 Cu T 200, Cu T 220 Cu T 380_A✓✓ - Cu T 380_{Ag} (+ silver) - Nova T Multiload Cu 250, Multiload Cu 375	5–10 yr
	With progestins (levonorgesterel ¤) **LNG-IUS** * Progestasert } most recent * Mirena, Levonova } but expensive ¤	1 yr 5 yr

Mode of action

1- Aseptic endometritis ¤ → histological changes in endomet. → hostile for fertiliz.

2- Uterine & tubal irritability (↑ PG) → interfere with sperm & ovum transport

3- If + Copper
- Inhibit *sperm* ¤ → affects motility & capacitation
- Inhibit *implantation* → affects endometrial metabolism
- Inhibit *zygote* → affects carbonic anhydrase (necessary to remove of CO_2)

Adv of adding Copper → it allows use of smaller IUDs (without loss of their efficiency)
Adv of adding Silver → it prolongs life span of IUDs (by preventing Cu fragmentation)

4- If + Progesterone
- Atrophic endometrium
- Thick, scanty, viscid cervical mucous (prevents sperm ascent)
- Prevents sperm capacitation

Advantages Φ
- One decision method & cheap
- Left for long periods & reversible on removal
- No systemic effects & no interference with intercourse or lactation
- Reliable (failure 1–2 /HWY ¤)......(0.2 in Levonova)
- Non-contraceptive benefits of **LNG releasing intrauterine system (IUS)** ⇔:
  - Treatment of dysfunctional uterine bleeding ¤
  - Prevention & treatment of endometrial hyperplasia
  - Protection from PID ¤

Contraindications (mainly local)

IUCD	▫ Distorted anatomy → fibroids, CMF of uterus ▫ Bleeding → severe anemia, bleeding tendency
Threads	▪ Pelvic infection (PID) or previous ectopic ▪ Immunosupression, steroids, DM, RHD (fear of IEC)
Cu^{++}	▫ Wilson disease
Undiagnosed	▪ Amenorrhea → suspect *pregnancy* ▪ Bleeding → suspect *malignancy*

Complications — 7 P — ΦΦ ✍✍

1) ***Bleeding***
   - Post-insertion spotting → reassure
   - Menorrhagia or metrorrhagia (25–50 % ↑)
     - *Etiology* → mechanical irritation of endom. → ↑ PG & fibrinolytics
     - *Treatment*
       - Exclude pathology 1st ✓
       - Anti-PG & anti-fibrinolytics (tranexamic acid)
       - If persistent → use a smaller or medicated loop
       - If still persistent → use another method

2) ***Pain***
   - Post-insertion (± vasovagal attack) → exclude perf. then reassure
   - Dysmenorrhea
     - *Spasmodic dysmenorrhea* is only accepted
     - *Otherwise exclude* →
       Large device, expulsion, perforation,
       infection, abortion, ectopic pregnancy

3) ***PID***
   - *Etiology* → septic technique during insertion (threads acts as a ladder)
     ↘ risk is slight ¤ : esp in the 1st month (actinomycosis israeli ¤)
   - *Proph.* → aseptic conditions, cut threads short (difficulty in removal)
   - *TTT* → remove IUCD (1st step) + strong antibiotics (acc. to C&S)
   - Vaginal disch / backache are common (pelvic congestion / chr cervicitis)

4) ***exPulsion***
   - 50% occur in 1st 3 months; esp during menses
   - *Pdf*
     - * If inserted postpartum / pregnancy occurs
     - * Too large / too small / bad technique on insertion
     - * Local abnormality of uterus / cervix
     - * Young age / nulliparity

5) ***Perforation*** **(rare ¤)**

- *Pdf* → same as above ↗
  (most imp is the reluctance / overconfidence of the doctor)
- *Suspected during*
  - Insertion → severe *persistent* pain & vaginal bleeding
  - Gradual perforation later on leads to:-
    - . PID (2^ry^)
    - . Missed threads
- *Management* → as in missed loop

6) ***Pregnancy***

▸ Intrauterine ⟹ i.e. failure (1-2 /HWY)

- Due to..................misplacement, perforation, expulsion
- Presents as.............*amenorrhea* → β-HCG + U/S
- There is risk of.......septic abortion, PROM, PTL
- Management:-
  - *If threads accessible* → remove ¤ ....25 % risk of abortion
  - *If not accessible* → continue ....50 % risk of abortion
    (with ↑ % of sepsis but no ↑ in % of CFMF)

▸ Extrauterine ⟹ i.e. ectopic (1-2 /10.000)

- *Etiology*
  - Associated tubal infection
  - Decreased tubal motility (as in mirena)
  - Good protection of intrauterine but not extrauterine preg.
  - ** Some say → IUD ↓ ectopic esp Cu T 380 A✓
    ↘ as it ↓ the overall rate of pregnancy
- *Management* → as in ectopic pregnancy + remove IUD

7) ***Missed threads*** (Missed IUD)

▸ Etiology - Adherence to vag wall, threads cut too short
  - *Expulsion, Perforation, Pregnancy*

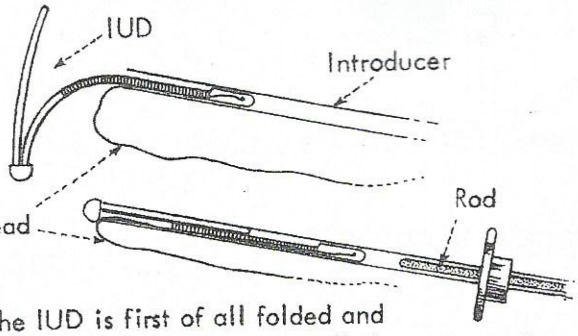
▸ IUD localization

- 1st step ⟹ try to find threads in vagina by speculum
- 2nd step ⟹ exclude pregnancy (U/S + pregnancy test)
- 3rd step ⟹ try to find it else where:-
  - Abdomen → plain X-ray (AP ± lat with uterine sound)
  - Uterus → hysteroscopy

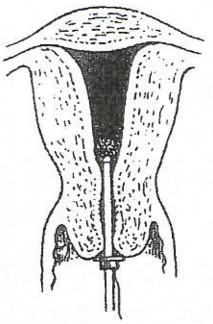
▸ Management

- If intra-uterine → hysteroscopic removal or D&C
- If extra-uterine → remove by LAPAROSCOPY ✓, minilaparotomy

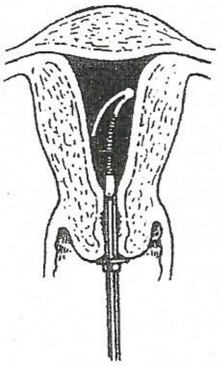
PRINCIPLE OF INSERTION OF IUDs



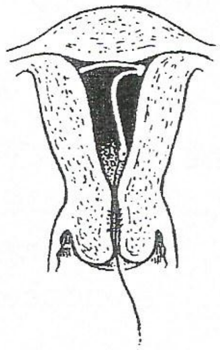
1. The IUD is first of all folded and pulled into a plastic tube called the introducer.



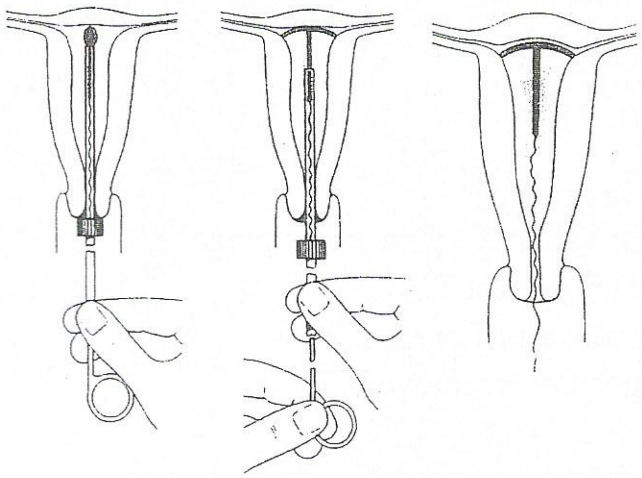
2. The introducer is then inserted into the uterus.



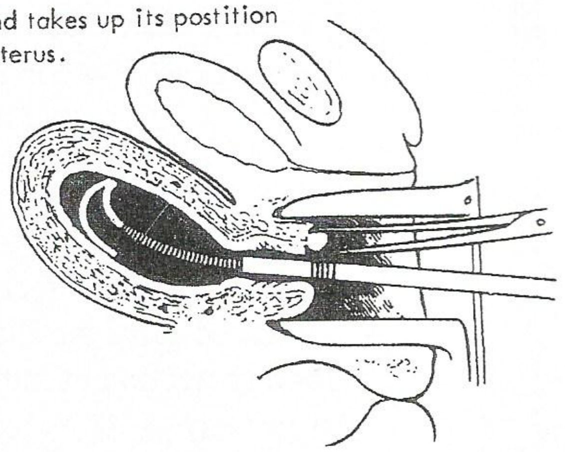
3. The IUD is forced out of the introducer by a rod.......



4. .....and takes up its postition in the uterus.



- Placement of an IUD.



KEY POINTS

1. IUDs are less well tolerated by nulliparous women but are ideal for the monogamous multiparous women for whom the pill is contraindicated.
2. The primary mechanism of action is a sterile spermicidal inflammatory response. Other mechanisms include inhibition of implantation and alteration in tubal motility.
3. The failure rates for IUD use are very low (<2%) with prolonged use but higher in the first year of use.
4. Potentially serious side effects include insertion-related salpingitis, spontaneous abortion, and uterine perforation.
5. The IUD provides protection against ectopic pregnancy while in situ.
6. The progesterone-containing IUD has the added benefit of decreasing bleeding and dysmennorhea.

Technique of insertion

Counsel the patient for

- Type / duration of IUCD
- Failure rate
- Warning signs
  - .....Missing threads / period
  - .....severe pain / discharge / bleeding

Timing

- Post-menstrual (cx is somewhat patulous, sure not preg.)
- Post-abortion (by one week)
- Post-partum (1st 48 hours or after puerperium)
- Post-coital (emergency) contraception

Mechanism

- Anesthesia.......................no need (just 2 supp. anti-PG)
- Position..........................lithotomy
- Bimanual examination........size, position, any contraindication
- Cusco speculum..............sterilize cervix by antiseptic solution
- Grasp anterior cx lip.......volsellum
- Uterine sound.................length & direction of uterus
- Two different techniques for insertion of IUCD:-

The push-out technique
  - Used for inert devices as Lippes loop
  - The inserter tip just passes the internal cervical os and the piston then pushes the device inside the uterus
  - The nylon threads are then... *cut 2-3 cm*...from the cervix

The withdrawal technique ✓✓
  - Used for copper devices
  - The inserter is introduced to reach near uterine fundus, then the outer sheath is withdrawn externally.
  - This technique... *reduces*... incidence of uterine perforation

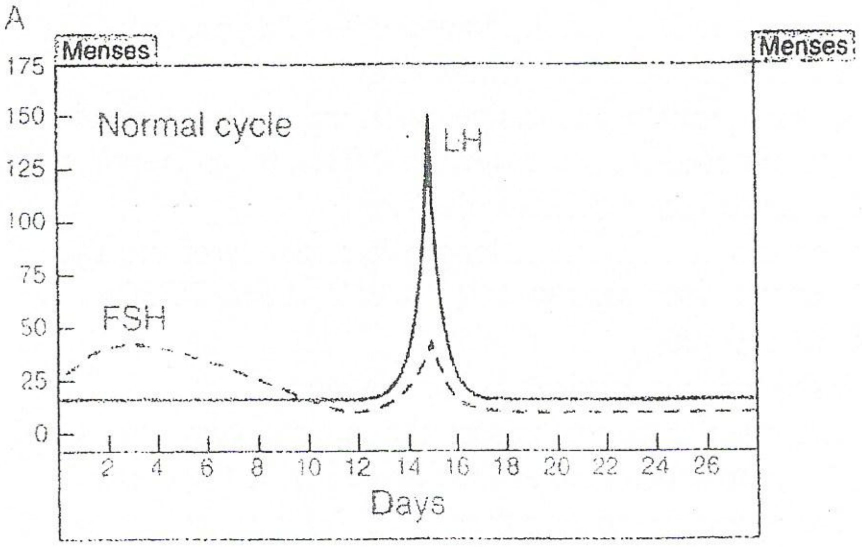
Follow up

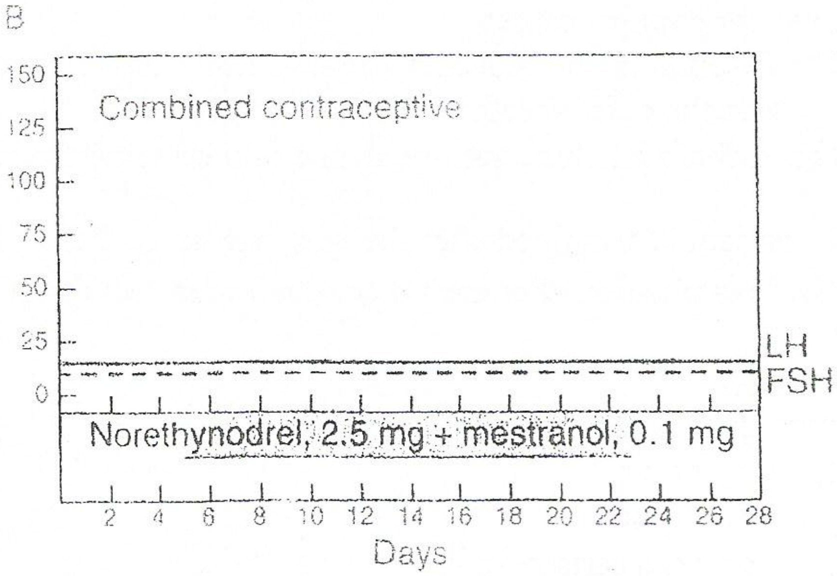
- The patient is examined after the *next menses* & then *every year*
- Self examination after each menstruation to feel threads

Indications of removal

- When pregnancy is desired
- If pregnancy occur
- If complications occur
- Each device has a certain ½ life
- After menopause (usually by one year)

Combined oral contraceptive pill preparations.





5] HORMONAL CONTRACEPTION

1. COC pills

Composition

E. used ⇨ . Ethinyl estradiol or
. Mestranol (Methyl EE). It has ½ potency of EE & requires removal of the methyl group in liver

P. (gestagen) used ⇨ similar to testosterone ¤

- 1st generation
  - *ESTRANE*...........Noresthisterone, Norethindrone, Norgestrel
  - *PREGNANE*........Medroxy progesterone acetate
- 2nd generation: Levonorgestrel
- 3rd generation: (new progestins) = ↑ potency + ↓ androgenic side effects ¤
  - Desogestrel..............***Marvelone***
  - Gestodene.................***Gynera***
  - Norgestimate...............***Cilest***
- 4th generation: drospirenone.......***Yasmin***

Types

① **Monophasic** ➡ all pills contain same concentration of E+P
according to E content → may be:
- High dose: 50 μg EE e.g. *ovral*
- Low dose: 35/30/20 μg EE e.g. *microvlar, norminest*

② **Biphasic** ➡ all pills contain E + P but pills taken last 11 days in the cycle have double P concentration e.g. *binovum*

③ **Triphasic** ➡ 3 types of pills but all contain E + P in different concentration (6+5+10) trying to mimic nature to ↓ side effects e.g. *trinovum*

Mode of action

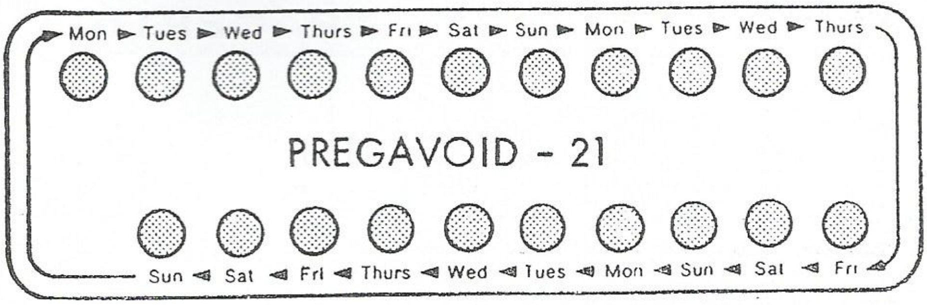
1) **Inhibition of ovulation** ✓✓
On hypothalamus: E → suppress FSH / P → suppress LH
On ovary: ↓ response to trophic hormones & ↓ steroidogenesis

2) **Unfavorable endometrium**
↓ size, vascularity, stroma → pseudo-atrophic state [P effect]

3) **Thick scanty cervical mucous** (interfere with sperm ascent) [P effect]

4) **Decrease tubal motility** [P effect]

5) **Inhibition of sperm capacitation** [P effect]



How late are you?

Less than 12 hours late → Don't worry. Just take the delayed pill at once, and further pills as usual. That's all.

More than 12 hours late →
- Take the most recently delayed pill now
- Discard any earlier missed pills
- Use extra precautions (condom, for instance) for the next 7 days

How many pills are left in the pack after the most recently delayed pill?

7 or more pills → When you have finished the pack, leave the usual 7-day break before starting the next pack

Fewer than 7 pills → When you have finished the pack, start the next pack next day, without a break

Interactions of Oral Contraceptives with Other Medications

Medications that Reduce the Efficacy of Oral Contraceptives	Medications Whose Efficacies are Reduced by Oral Contraceptives
Penicillins	Folates
Tetracycline	Anticoagulants
Sulfonamides	Insulin
Rifampin	Methyldopa
Ibuprofen	Hypoglycemics
Phenytoin	Phenothiazides
Barbiturates	Tricyclic antidepressants

▸ Advantages ΦΦ

* Contraception

- Failure rate = 0.1 / HWY (most effective method) ¤
- Cheap, easy to use, not related to intercourse, rapidly reversible ¤

* Non contraceptive benefits ¤

- Control of dysfunctional uterine bleeding
- Decreased menorrhagia → decreased anemia ¤
+ Dysmenorrhea & Premenstrual tension decreased
+ Endometriosis, fibroids, endometrial carcinoma (NB → cr cx little↑ ¤)
+ Functional ovarian cyst, ovarian carcinoma
- Decreased PID (thick cx mucus) but doesn't protect against STD ¤
- Suppression of lactation & ↓ benign breast lesions

▸ Pill administration

Choice of pills → better to use

- Low dose E pills (less E side effects with same potency)
- Triphasic pills (more similar to natural cyclic changes)
- New (3rd generation) containing pills (less A side effects)

Starting pills

- From day 2–5 of cycle one tablet is taken daily for 21 days then stop 7 days → menstruation (after 2-3 days). Then repeat
- May start from the 1st day of cycle → better protection
- The 28 pack contains 7 days of iron (norminest Fe)
- May start 4 week after labor (non-lactating)
  ↘ or 1 week after abortion

Missing pills

- If 1 pill is forgotten → take <u>one</u> as soon as possible then the next pill is taken at usual time
- If 2 pills are missed → as above but
  ↘ extra-precaution backup for the rest of cycle (e.g. condom)
  ↘ if < 7 pills are remaining in the pack → start another pack next day…(thus omitting the usual 7 day free interval)

Drug interactions

* Drugs → ↓ pills ¤ (sedatives, anti-epileptics, anti-histaminic, antibiotics ✓)
* Pills → ↓ drugs (anticoagulants, antidiabetics, antihypertensives)

Side effects & Complications

▸ **CNS** [P effect]
- *Headache & migraine*
- *Mood changes* → depression & irritability

▸ **CVS**
- 'E' *effect* → liability to thrombosis ✓ (effect on clotting factors)
- *P* effect . Astherosclerosis (effect on lipid profile)
  . Hypertension (salt & H_2O retention & ↑ renin-angiotensin)

▸ **Breast** ['E' effect]
- *Breast engorgement & mastalgia*
- *Decreased milk production*
- *Cancer breast* . Premenopausal → very little risk (esp if use > 10 yrs)
  . Postmenopausal → risk is less & even may drop

▸ **GIT** ['E' effect]
- *Nausea & Vomiting* → esp on 1st few weeks
- *Liver* → . *Tendency to cholestasis, gall stones, may affect liver enzymes*
  . *Very rarely* → *hepatocellular adenoma* ¤

▸ **Metabolism**
- *CHO metabolism* → insulin antagonism ['E'+ P effect]
- *Weight gain* [salt & water retention or anabolic effect of P]

▸ **Menstrual**
- *Hypomenorrhea* → usually improves menstrual control ¤
- *Amenorrhea*
  - Exclude pregnancy (β-HCG + U/S) then → start pills after 7 d
  - If persistent for 2–3 months → postpill amenorrhea
- *Spotting*
  - If occasional → reassure (inappropriate hormone content of the pill)
  - If early → use pill with more estrogen
  - If late → use pill with more progesterone
  - Also may take 2 pills for rest of the cycle
- *Breakthrough bleeding*
  - Stop pills 5 days then restart (+ backup contraception for 2 wks)
  - Or use pills with more estrogen
- *Change in libido / Leuchorrhea* (pelvic congestion)

▸ **Skin**
- ↑ *Pigmentation* → chloasma ['E' +P]
- *Acne, hirsutism* → *recently improved* ¤ (with 3rd generation e.g. Diane)

Contraindications (*absolute....or....relative*)

- **CNS**
  - Migraine
  - Epilepsy (COC → decrease anti-epileptic drug efficacy)
  - o Otosclerosis
  - o Optic neuritis & glaucoma
  - Porphyria ¤
  - Persistent visual symptoms esp if suggestive of TIA

- **Cardiovascular**
  - Patients with history of thrombosis, pulmonary embolism, coronary heart disease..........................absolute #
  - Patients with risk of thrombosis as
    - Prolonged immobilization
    - Before and after surgery (4–6 wks)
    - Sickle cell disease or sickle 'C' disease ¤
    - Varicose veins
    - History of myocardial infarction in a parent
  - Hypertensive patients
  - All patients > 45 years
    Patients > 35 years if they are *smokers* or *obese*

- **Lactation** ¤ + **suspected breast cancer**..............absolute #

- **Liver**
  - Markedly impaired liver function, history of cholestasis during pregnancy, adenoma ....absolute #
  - Hyperlipedemia (E → increases triglycerides)

- **Diabetes mellitus** + **thyrotoxicosis**

- **Local conditions**
  - Pregnancy:
    - No evidence of teratogenic effect
    - Very rarely → VACTREL syndrome (P)
  - Undiagnosed amenorrhea
  - Undiagnosed bleeding

2. POP (Minipills)

Preparation

Pills containing very small amount of Progesterone

- Levonorgestrel ⇨ **Microlut** (30 µg)
- Noresthisterone ⇨ Micronor (350 µg)
- Lynestrenol ⇨ **Exluton**

Mode of action

- On cervical mucous → thick ✓✓
- On endometrium → atrophy
- On sperms → inhibits capacitation
- To less extent → alter tubal motility & suppression of ovulation (50%)

Use (35 tablet /pack)

1 tablet is taken DAiLY from the 1st day of the cycle CONTInuOUSLY at the same time¤. If forgotten or DELAYED ≥ 3hr→ continue backup 14 ds

NB......Cerazette is a NEW GENERATION "desogestrel"¤
↘ could be delayed up to 12 hours safely

Indications

1. *Lactating*
2. *As there is no estrogen side effects:*
   - CVS.........Liver
   - Old ¤......smoker ¤
3. *As there is min. Prog. effect (e.g. CHO, lipid metabolism, weight gain)*
   - Diabetics & hypertensive
   - Obese

Disadvantages & side effects

- Higher failure rate than combined pills = 1–2 /HWY ¤
- Liability to ectopic pregnancy (due to effect on tubes)
- Menstrual side effects e.g. Spotting or Irregular cycles
  - ↳ use another type with more progestin
  - ↳ but don't use estrogen as it interferes with progesterone action on mucous & endometrium

Contraindications

- Undiagnosed amenorrhea
- Undiagnosed ¤ genital bleeding
- Previous *ectopic* pregnancy

⚜ 3. Injectables ⚜

Preparation ➟ Depot Medroxy-progesterone acetate
= Depo-Provera 150 mg IM / 3 months ¤
➟ **Combined (E&P)... See below**

Mode of action

The *same* as COC ¤ (--,--,--,--,--)......mainly by thick cx mucous ¤

∴ *Reliable* as COC (>99%)

∴ *Non-contraceptive benefits*

- Endometriosis, endomet. hyperplasia or carcinoma
- Improves PMT & dysmenorrhea
- Precocious puberty, hirsutism
- Protects against PID (but not STD ¤)

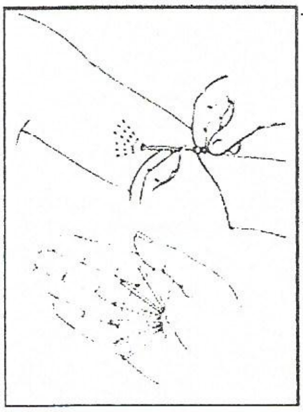
Indications

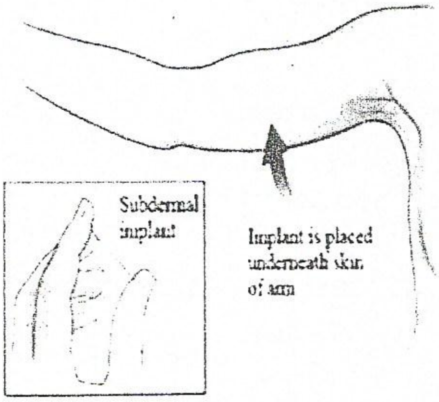
1. *Lactating* (with no ↑ in cancer breast)
2. *As there is no estrogen side effects:*
   - CVS.........Liver
   - Old ¤......smoker ¤

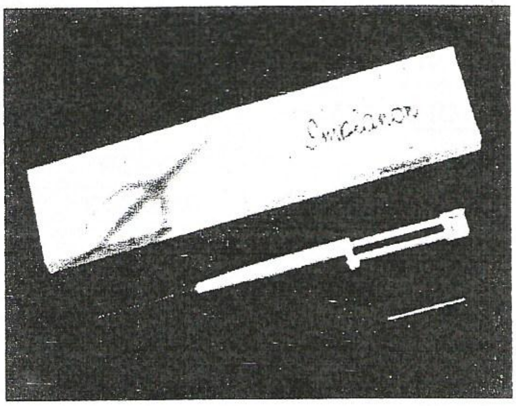
Disadvantage & side effects ΦΦ

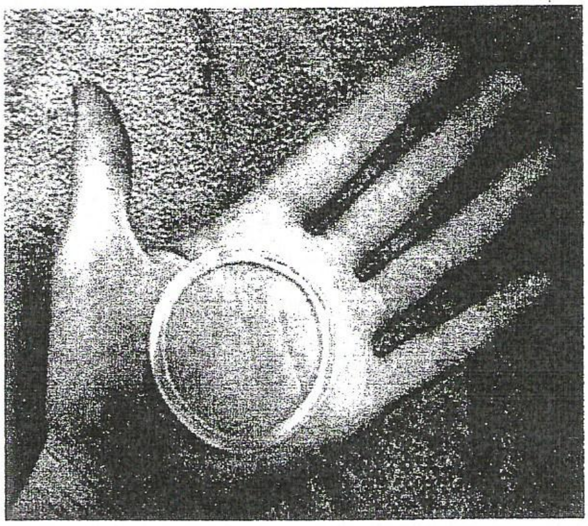
- *Can't reverse contraception* once injection started (may take up to 9 m)
- ↑ *Risk of osteoporosis if used in younger age* ¤ (reversible)
- *As there is Prog. effect*
  - Weight gain in some patients ¤
  - Few metabolic effects → mild anti-insulin action, Decreased HDL-C
- *Menstrual irregularities* (most common ¤) ✓
  - Amenorrhea → 70% by the end of 1st year
  - Oligomenorrhea / hypomenorrhea → reassure
  - Irregular bleeding → exclude pathology then give:-

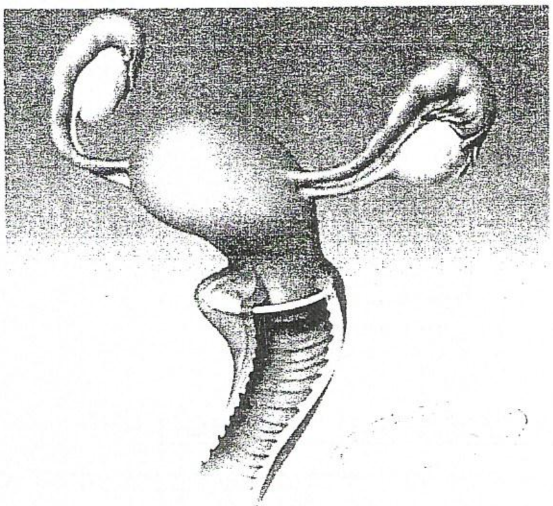
1. **Take next DMPA injection before date,** or....
2. **Noresthisterone oenanthate (NET-EN)**
   ↳ Norstrat or Norigest 200 mg IM / 2 months
3. **Recently: monthly combined injectable contraception**
   ↳ **Cyclofem** (DMPA 25 mg + estradiol Cypionate 5 mg)
   ↳ **Mesygyna** (DMPA 50 mg + estradiol valerate 5 mg)
   ....E was added to ↓ menstrual side effects.........
   ....but it thus has same adv/disadv as in COC ......




Subdermal implant
Implant is placed underneath skin of arm


Implanon





⚜ 4. Subdermal Implants ⚜

Method (Norplant)
- SIX cylinders containing Levonorgestrel ¤ (36 mg / cylinder)
- Inserted SC on inner aspect of medial side of arm in a fan shaped manner
- Slow release of progestin → lasts for five years

Action → as POP ¤

Adv → . Long acting (99% protection ¤)
. Action is rapidly reversible ¤ after removal
. No side effects of estrogen

Disadv → . Headache / breast tenderness / weight gain
. *Menstrual irregularities* / amenorrhea (the cause of removal)
. Difficult insertion & removal (needs provider's help)

NB → *Implanon* is a SINGLE cylinder left for 3 years ✓✓ "etonogestrel" ¤
↘ it recently replaced Norplant (FDA approved 2006)

⚜ 5. Vaginal contraceptive ring (VCR) ⚜

Combined vaginal ring (EE + Levonorgestrel)
As COC (inserted for 3 weeks & removed for 1 week)
(Failure rate = 0.5 / HWY)

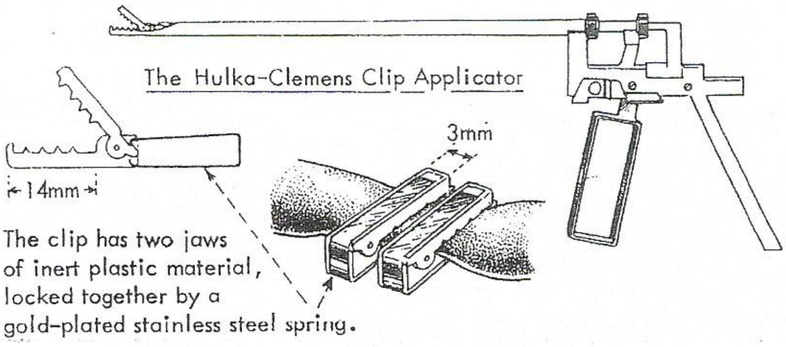
Progesterone-only vaginal ring (Levonorgestrel)
. Used monthly or every 3 month
. Less effective

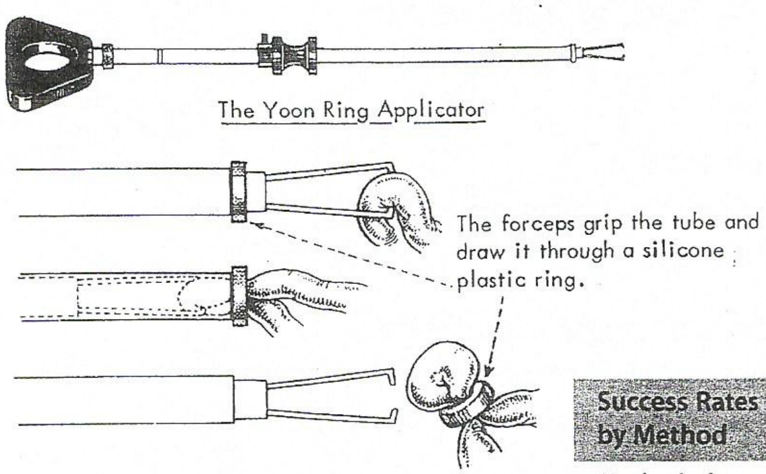
⇨ Advantage of vaginal rings
- Immediately reversible
- Simple introduction & removal
- Fewer side effects (bypass 1st effect of hepatic metabolism)

⚜ 6. Combined hormone patches ⚜

⇨ Evra patch for 3 wks and then removed 1 wk
⇨ Failure rate 1.2 /HWY

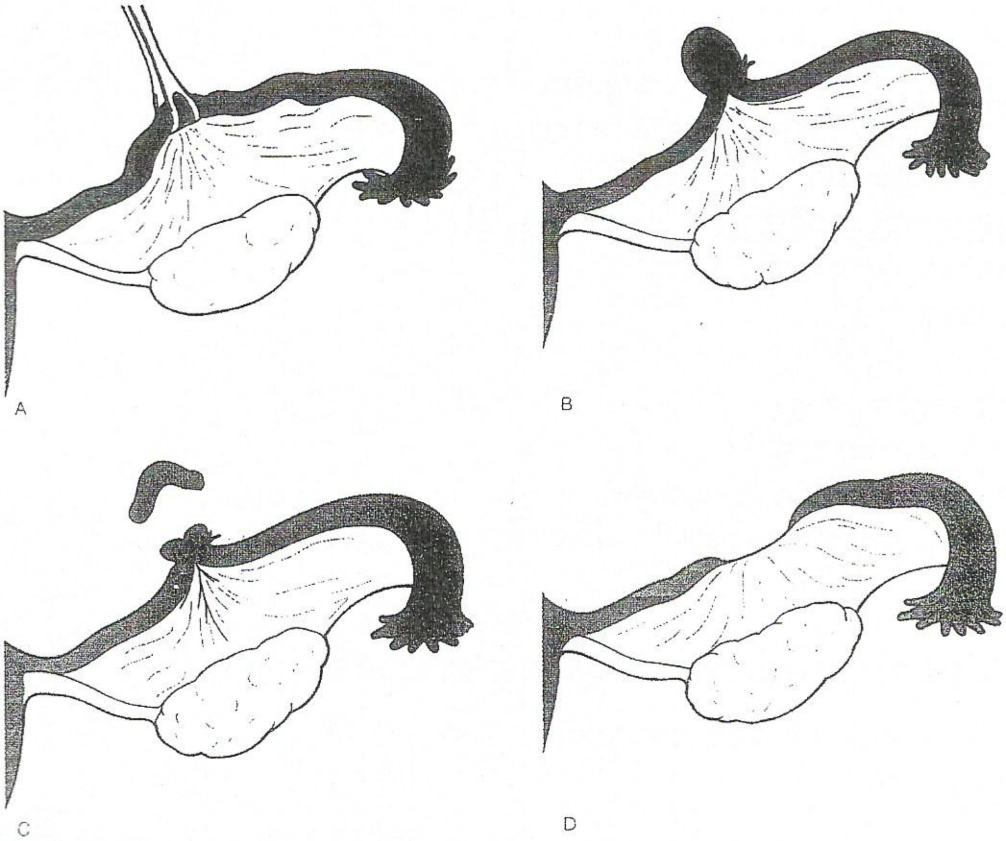
⚜ 7. P.releasing IUCD ⚜





Success Rates of Tubal Occlusion Reversal, by Method

Method of Tubal Sterilization	Success Rates for Reversal (in %)
Clips	84
Bands	72
Pomeroy	50
Electrocauterization	41



• A–D: The Pomeroy method of tubal sterilization. This technique is typically performed during the immediate post-partum period through a small subumbilical incision.

6] SURGICAL (STERILIZATION)

Types

1) Male ➟ Bilateral Vasectomy

- Done under local anesthesia } v. easy but
- Use another method for 70 days } not ....
- Efficiency confirmed by 2 -ve semen analysis } in Egypt

2) Female ➟ Tubal Ligation

- *Laparoscopy* ✓ electrocoagulation of tube or application of a Falope *ring* or *clip*
- *Minilaparotomy* resection ligation of a part of the tube (POMEROY method)
- *Postpartum*
  - At C.section (common)
  - After VD (2–3 days later via a small sub-umbilical incision)

Indications

ς permanent contraception:

- Completed family, old couple (> 35) → with failed all other methods
- Contraindication for pregnancy → v. weak scar, v. serious illness

Contraindications

ς as reversibility is difficult:

- Young uncertain couple with marital or mental problems

Complications

- *Complications of anesthesia* or *surgery* (infection, bleeding, bowel injury)
- *Pregnancy (Failure)* → 0.1-0.4 / HWY due to
  - Recanalization (esp. postpartum: large vascular tube)
  - Faulty technique
- *Post-ligation syndrome*

  Menorrhagia & congestive dysmenorrhea months or years after the procedure. Mostly due to interference with OVARIAN venous return → congestion

Male contraception Φ

Permanent ➟ vasectomy

Temporary ➟

- Physiological..........coitus interruptus & interfemoris
- Mechanical...........male condom
- Chemical..............*Gossypol* (inhibits mitochondria & motility)
- Hormonal.............progesterone / danazol / LHRH analogues
- Immunological.......contraceptive vaccines against sperms

Immunological contraception

- Antibodies (passive) or antigen (active) for
- Sperms / zona pellucida / HCG

Postpartum contraception Φ

- Immediately
  - ↘ Breast-feeding, Barriers, sterilization
- Lactating women at 6 wks
  - ↘ Progestagen only methods (POP, DMPA, implants)
  - ↘ IUCD
- Lactating women at 6 months
  - ↘ Methods containing E (COC, combined monthly injectable, VCR)

Postcoital (emergency) contraception

- Hormones
  - ς Given immediately or within 72 hours ¤ (the morning after-pill) ¤
  - ς Large doses → N&V → antiemetic must be added ¤
  - ς They inhibit ovulation + early luteolysis (interception)

- **POP** e.g. Postinor (750μg levonorgestrel): 1 tab.......repeat after 12 hrs
- **High dose COC** e.g. Ovral: 2 tablets.....................repeat after 12 hrs
- **Anti-gonadotrophin** e.g. Danazol 600 mg..............repeat after 12 hrs
- **Anti-progesterone** e.g. ellaOne 30 mg tab............................once

- Mechanical
  - **IUCD** is inserted immediately even up to one week ¤. FR = 1 %
  - **Menstrual aspiration** → suction of the uterine contents by Karman cannula

Special groups

	IUCD	COC	POP
	Barriers & sterilization are available offer for all		
DM	✗ risk of PID	✗	✓
Cardiac	✗ risk of IEC	✗	✓
Newly married	✗ difficult insertion	✓ the best	
Lactating	✓	✗	✓
Elderly (>40)	✓	✗	✓

Contraindications for pregnancy

- Mother → High risk preg (DM, heart)
  - → Infection (Rubella).....Vaccination (MMR)
  - → Drugs (e.g. acne therapy with retinoic acid – 6 m at least)
- Uterus...scarred with liability to rupture

Counseling before starting contraception

- Method……………………………cost, duration, failure rate, reversibility
- Technique……………way of usage / missing-discontinuation / removal
- Patient…………advantage /disadvantage/ contraindication /side effects

WHO Medical Eligibility Criteria (WHO.MEC)

1	***No restriction***	Use the method ✓✓
2	Advantage of usage **overweighs** theoretical /proven risk	
3	Theoretical /proven risk **overweighs** using contraception	Do not use the method ✗
4	***Not recommended***	

<u>WHO-MEC has replaced the old classification into indications / relative contraindications / absolute contraindication</u>

	Not use	May use
COC	- Heavy smoker - Severe HTN, complicated DM - Active liver disease / cirrhosis/ liver tumors - Pregnancy Lactating during first 6 wks - Unexplained vaginal bleeding, Breast cancer - Migraine, epilepsy - Thrombo-embolic/ Ischemic/ Valvular lesions	- >35 yrs, mild smoker - Mild / mod HTN, controlled DM - Gall bladder disease - Lactating from 6 wks till 6 ms Non-lactating during first 3 wks - Current ttt with antibiotics:- Rifampicin / Griseofulvin Antiepileptics
POP	- Pregnancy / Lactating during first 6 wks - Active liver disease / cirrhosis/ liver tumors + Gall bladder disease - Unexplained vaginal bleeding / Breast cancer - Current ttt with antibiotics:- + Rifampicin / Griseofulvin + Antiepileptics	
Inject. (prog. only)	- Pregnancy - Unexplained vaginal bleeding - Breast cancer	- Lactating during first 6 wks - Severe HTN, complicated DM - Thrombo-embolic/ Ischemic /stroke history - Active liver disease / cirrhosis/ liver tumors
IUCD	- Current / recent:- PID, STIs, septic abortion, pelvic TB - Pregnancy / Distorted uterine cavity - Unexplained vag bleeding / genital tumors	- Risk of developing STIs - HIV / AIDS infection

Chapter 5 Infection

Vaginal discharge

Sexually transmitted disease

Vulvovaginitis

Cervicitis

Pelvic inflammatory disease

Chronic granulomatous disease

	G +ve	G –ve
Aerobes	**Lactobacillus** **Staph aureus, strept** **Enterococcus faecalis** **Diphteroids**	**E-coli** **Klebsiella, proteus** **Enterobacter** **Pseudomonas**
Anaerobes	**Peptostreptococcus** **Clostridium** **Lactobacillus** **Gardnerella vaginalis** **Yeast (candida)**	**Bacteroids** **Bacteroids fragilis** **Fusobacterium**

Normal vaginal flora

Organism	Percentage
Lactobacilli	80–90
Staphylococci, micrococci	50–70
Ureaplasma	40–50
Anaerobes	20–50
Streptococci	20–30
Gardnerella	10–30
E. coli	5–15
Candida spp.	5–15
Bacteroides	5–10
Trichomonas	3–7

Vaginal discharge

Leucorrhea is clear mucoid (non-infected) vaginal discharge d.t. excess ¤ of normal secretions. (*Some say* leucorrhea means **any** *abnormal* discharge from vagina except *blood*)

Normal vaginal discharge ➩

	PH ¤	SOURCE
VULVA	Alkaline	Bartholin gland ± Skene's glands
VAGINA	ACIDIC (3.8 – 4.2)	Serous transudate + Bartholin + cx mucus
CERVIX	Alkaline (8.5)	Endocervical glands (↑ed by 'E' → CYCLIC)
UTERUS	Alkaline	Endometrial glands (esp secretory phase)
TUBES	Alkaline	Goblet glands

Normal bacteria flora ....a balance of ....
- *Lacto-acidophilus bacilli* ✓✓ (Doderlein bacilli, g+ve rods)
- *Strept., staph., E-coli*
- *Candida, Trichomonas, mycoplasma, g-ve anaerobes, diphteroids*

Normal defensive mechanism

Vagina → . Closed mechanically by the 2 labia (opposed¤)
. Lined by thick stratified squamous epithelium ¤
. *Acidic* ¤ media → hostile for organisms (lost by ➊+➋+➌+intercourse)

Cervix → closed mechanically by a mucous plug

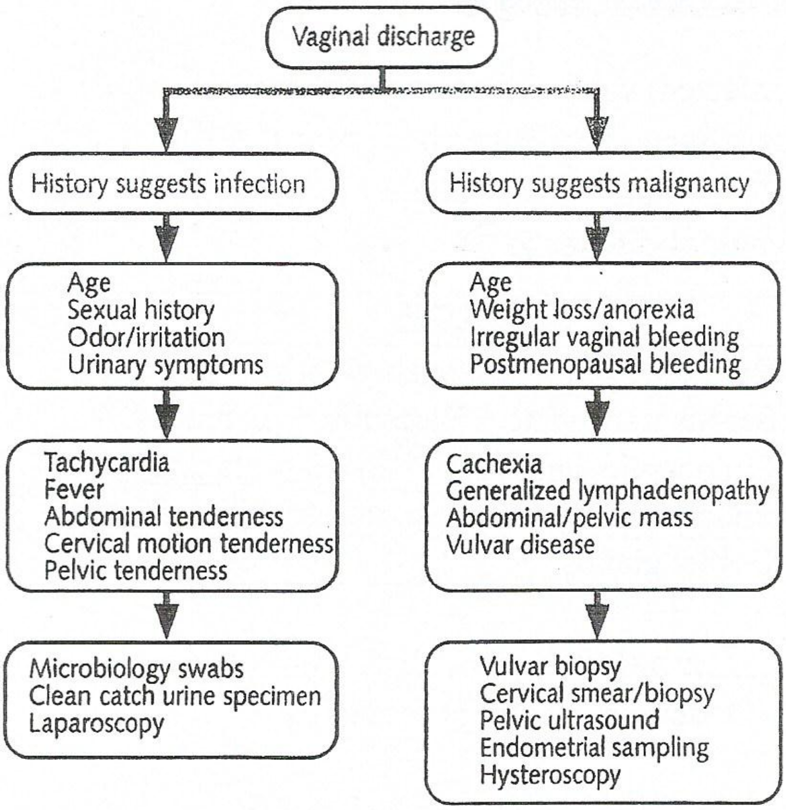
Uterus → monthly shedding of superficial layer of endometrium

Tubes → movement of cilia towards uterine cavity

This mechanism is interfered with at

- Prepubertal & postmenopausal
  - Less acidic pH ➊
  - Thin vaginal lining
  - No endometrial shedding
- Menstruation
  - Less acidic pH (neutralized by alkaline menses) ➋
  - Loss of cervical plug
- After labor & abortion
  - Less acidic pH (neutralized by alkaline lochia) ➌
  - Loss of cervical plug (& cervix is opened)
  - Presence of raw placental bed (± lacerations)
  - Lowered maternal resistance (d.t. exhaustion)
  - No endometrial shedding

Algorithm for vaginal discharge.



Work-up of vaginal discharge

Investigation	Cause of discharge
Microbiologic swabs	Wet mount *Candida albicans* *Trichomonas vaginalis* Bacterial vaginosis Endocervical/urethral swab *Chlamydia trachomatis* *Neisseria gonorrhoeae*
Clean catch urine specimen	Infection
Cervical cytology	Cervical disease
Endometrial sampling/ hysteroscopy	Uterine disease
Pelvic ultrasound	Pelvic mass
Laparoscopy	PID Pelvic malignancy

Classification

According to Source

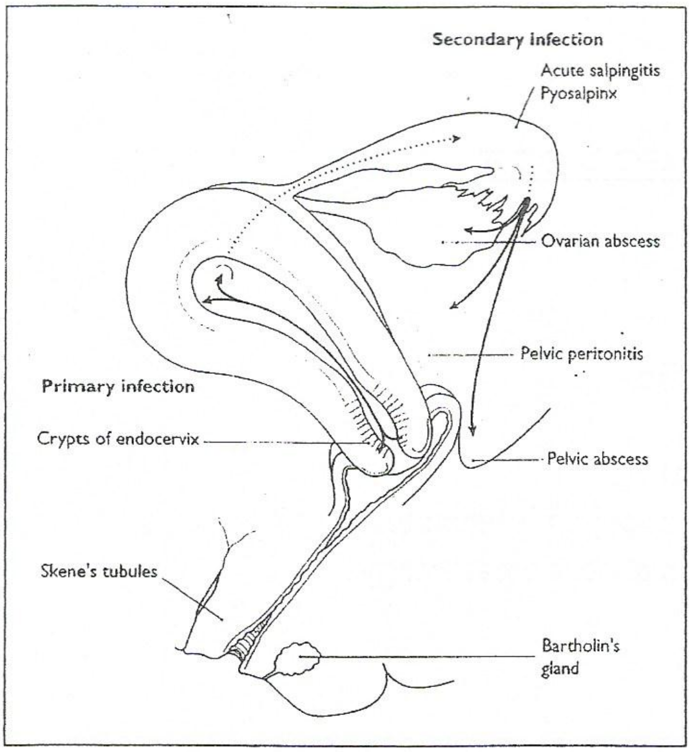
1. **True leucorrhea** (↑ed normal secretions or transudation)
   - Hormones (esp estrogen)
     - . **P**uberty
     - . **P**remenstrual & midcyclic
     - . **P**regnancy
     - . **P**uerperium (lochia alba)
   - **P**elvic CONGESTION (constipation, coitus interruptus, sexual dissatisfaction ± pelvic pathology)

2. **Pathologic causes**

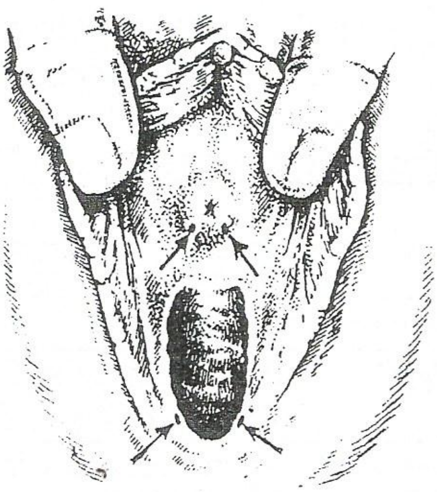
	Vagina	*Cervix*	*Uterus*	*Tube & ovary*
Trauma	F.B., pessary	ulcers, erosions	IUCD	Tubal ligation
Infection	-Bact. vaginosis -TV & monilia	Cervicitis: acute / chronic	-Endometritis -Pyometra	-PID -Pelvic abscess
Neoplasm	vaginal adenosis	infected tumors e.g. cr endomet., fibroid, polyps		
Miscellan.	Fistula		- Fistula - ROM, VM	Intermittent hydrosalpinx

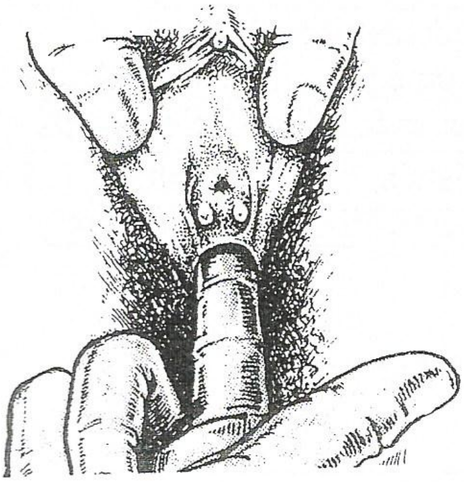
According to Character

Whitish	- True leucorrhea - Monilia	**Yellowish** (greenish)	- T.V. - Bacterial vaginosis
Mucoid	. Vaginal adenosis . Cervicitis	**Serous** (watery)	. ROM . Urinary fistula . Intermittent hydrosalpinx
Muco-purulent	- Vulvo-vaginitis - Bartholinitis	**Purulent**	- Endometritis, pyometra - PID, P. abscess if opens into vag
Sanguin-eous	. Foreign body . Vag., cx, uterine → ulcers, erosion polyps, cancer	**Offensive**	. Trauma → retained F.B. . Infection → p. sepsis, p.abscess . Neoplasms → infected tumors . Fistula → recto-vaginal fistula



Route of spread of non-gonococcal and gonococcal infection.





EXAMINATION

The labia are held apart, and the urethra, Skene's ducts and Bartholin's ducts examined for signs of infection. These ducts should be 'milked' for specimens of pus, if any, and swabs are taken from the cervix which is the main reservoir of infection.

KEY POINTS

1. *N. gonorrhoeae* causes a reported 2 million infections per year.
2. Common conditions caused include cervicitis, PID, TOA, and Bartholin abscess.
3. Diagnosis can be made with culture, Gram's stain, or DNA probe.
4. Treatment for uncomplicated infections is ceftriaxone 250 mg intramuscularly once.
5. Treatment for *N. gonorrhoeae* should always include doxycycline 100 mg orally BID for 1 week to treat likely concomitant chlamydial infections.

Sexually Transmitted Diseases

❶ Gonorrhea

▸ Etiology

Cause → gonococcus (gram –ve intracellular diplococcus)
Transmission → sexual intercourse……incubation period: 3–7 d

▸ Clinical picture

Primary sites (∇) ⇨ ❶ Skene's glands & urethra
❷ Bartholin gland
❸ Endocx (angry red cervix + mucopurulent discharge)
↘ the main reservoir of organism

Other sites ⇨ ❶ Rectum → proctitis
❷ Pharynx (oral sex) → pharyngitis
❸ Eye → ophthalmia neonatorum / conjunctivitis in adults

Spread

- Local → . Vulvovaginitis (only prepubertal or postmenopausal)
  . PID, pelvic or generalized peritonitis
  . Perihepatitis → Fitz-Hugh-Curtis (FHC $)
- General → septic arthritis, meningitis, endocarditis

▸ Investigations (C&S)

- *Smear* → endocervix, rectum, pharynx
- *Culture* → on Thayer-Martin ¤ or New York City medium
- *Antigen detection* from 1ry sites → ELISA / NAAT (nucleic acid amplification test)
- *Serology* → CFT / HAI

▸ Treatment

1] Uncomplicated ⇨ acute gonorrhea…….*CDC recommendation…*

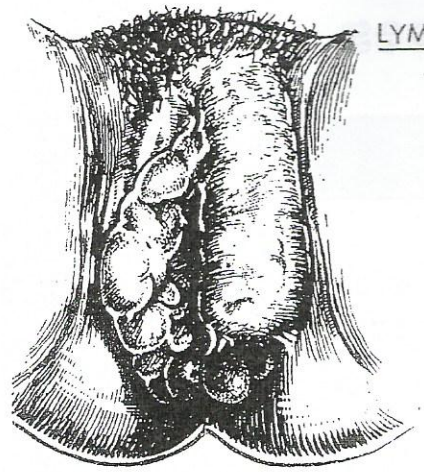
Cephalosporins: ceftriaxone 250m IM or cefixime 400 mg orally (single dose)..**or**
Quinolones: ciprofloxacin 500 mg or ofloxacin 400 mg orally (single dose)..**or**
Azithromycin: 2 g orally (single dose)…………**Plus**
Doxycycline: 100 mg / 12 hrs orally for 7 days if co-infection with Chlamydia ¤

Previously ♦*Procaine penicillin* 4.8 million units IM once ± Probenicid
♦*Spectinomycin* 2g IM ¤
♦*Tetracycline* or *erythromycin* if resistant/ allergy to penicillin

2] Complicated ⇨ chronic gonorrhea e.g.

- *Chronic cervicitis* → cauterization
- *Bartholin abscess* → drainage
- *Chronic PID* → adenexectomy

LYMPHOGRANULOMA VENEREUM (LVG)



The picture shows an advanced case of LGV.

KEY POINTS

1. Chlamydial infections tend to coincide with gonococcal infections. However, the incidence of gonococcal infections has decreased, whereas the incidence of chlamydial infections has increased.
2. Many chlamydial infections are entirely asymptomatic.
3. Treatment is with doxycycline 100 mg BID; alternatively, a one-time 1 g dose of azithromycin can be used.
4. LGV is caused by the L-serotypes of *Chlamydia*.

❷ Chlamydia

Bacteriology (incubation period → 1-2 weeks)

- SIMILAR TO VIRUS IN → obligatory intracellular¤ + inclusion bodies
- SIMILAR TO BACTERIA IN → . two types of nucleic acid
  . divides by binary fission
  . sensitive to some antibiotics

* It affects **5%** of females

* However, it is asymptomatic in **50%** ¤

Serotypes (15 ?!)

↳ **A, B, C.........Trachoma**

↳ **D-K............considered the commonest ¤ STD ✓**

- On ♀ ➟ cervicitis, Bartholinitis, **PID** (more insidious / worse course than Ğ)
- On PREGNANCY ➟ abortion, PROM, PTL, intrauterine infection
- On newborn ➟ ophthalmia neonatorum, pneumonia
- On ♂ ➟ urethritis (sterile pyuria¤), epididymitis, conjunctivitis

↳ **L1, L2, L3..........lymphogranuloma venereum**

- Vulva, VAGINA, CERVIX ➟ single or multiple papules, vesicles or pustules → ulcers → fibrosis, stricture & fistula
- LYMPHADENOPATHY (bubo) ➟ suppuration, matting together, sinuses
- CHRONIC LYMPHANGITIS ➟ obstruction, edema, fibrosis, elephantiasis
- PROCTOCOLITIS ➟ diarrhea, fibrosis, strictures & fistula

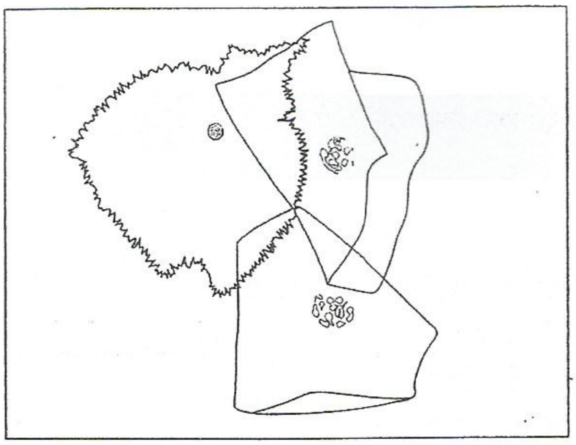
Investigations

- *Smear* → intracellular inclusion bodies + >10 pus cells / oil immersion field
- *Culture* → on tissue culture (MacCoy).............. the most *reliable* (but takes ⏲)
- *Antigen detection* → . ELISA.......................................the most *rapid*
  . PCR –using NAAT technique–........the most *expensive*
- *Serology* → micro-IFT¤, CFT

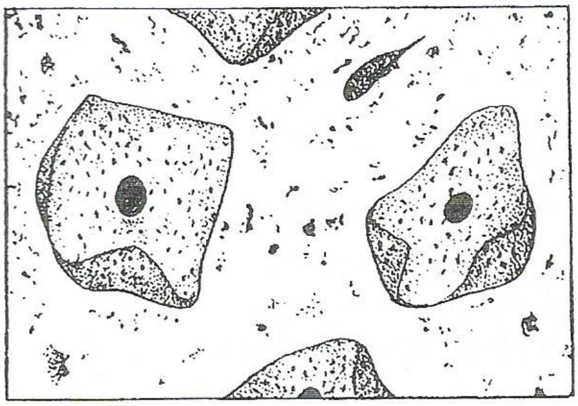
Treatment ....*CDC recommendation*.........

Azithromycin: ¤ 1 g orally once (suitable during pregnancy)......................or
Doxycycline (vibramycin): 100 mg/12 hrs orally for 7 days (not in pregnancy)....or
Quinolones: as ofloxacin: 300 mg/12 hrs orally for 7 days (not in pregnancy)

- *Screening for high risk asymptomatic cases* ⇨ sexually active < 25 yrs, multiple partners, history of previous / other STD
- *Abstinence from sexual intercourse* ⇨ till complete therapy
- *Clindamycin/ Erythromycin/ Tetracycline* were used for both ⇨ chlamydia & Ğ



'Clue cells', seen in Bacterial vaginitis.



A smear infected with G. vaginalis. Note the 'clue cells', vaginal epithelial cells stippled with small coccobacilli.

KEY POINTS

1. Bacterial vaginosis is polymicrobial but usually attributed to *Gardnerella*.
2. The discharge is usually thin, yellow, and has a characteristic "fishy" amine odor; the whiff test exaggerates this odor with KOH.
3. Formal diagnosis is made by visualizing clue cells on wet prep.
4. First-line treatment is metronidazole (Flagyl) for a 7-day course.

❸ Bacterial (non-specific) vaginosis

Gardnerella vaginalis
(Haemophilus vaginalis)

▸ DEFINITION

Bacterial vaginosis means replacement of normal vaginal flora (Doderlein bacilli) by other bacterial colonies (mainly *G.vaginalis, mycoplasma*¤ *hominis, ureaplasma urealyticum*)

Incidence → 10–25% of population (✓✓60% of vulvo-vaginitis ¤)

Predisposing factors (alkaline medium)

- Frequent sexual intercourse ¤
- Frequent use of alkaline vaginal douches

▸ CLINICAL PICTURE

- *Asymptomatic* (50%¤)
- *Mild vulvo-vaginitis* → no PPdd (…osis & not…itis) → no pus cells ¤
- *Vaginal discharge* (profuse, thin, greyish, malodorous)

(Fishy odor¤ is due to formation of amines from a.a. by anaerobic bacteria especially apparent after intercourse or menstruation)

▸ INVESTIGATION ¤

(❸ of the ❹ AMSEL criteria are enough)

1] ***Characteristic vaginal discharge***
2] ***Vaginal pH > 4.5***
3] ***Clue cell*** (granular appearance of vaginal epithelial cells due to adherence of bacteria to their surface). Demonstrated by:
- Gram stain → gram -ve cocobacilli (H. vaginalis)
- Wet smear → drop of saline + drop of vag. discharge

4] ***Whiff test*** (add 10% KOH → fishy odor)

▸ COMPLICATIONS:

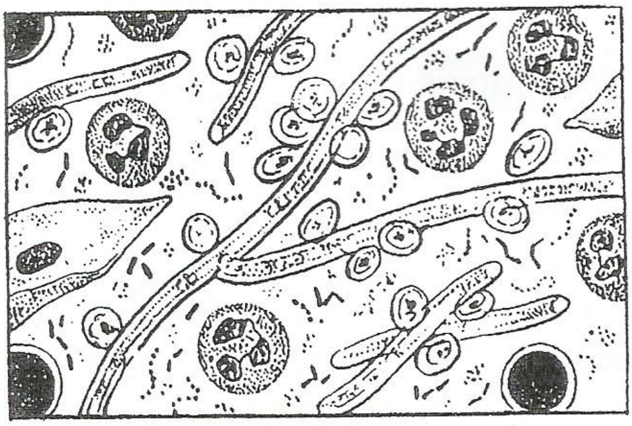
☆ **Pdf for infection in :-**

- Non-pregnant → chronic PID, UTI
- Pregnant → chorioamnionitis, PROM, PTL
- Wound infection after surgery e.g. vag. cuff after hysterectomy

☆ **However, there is no general agreement on prophylaxis**

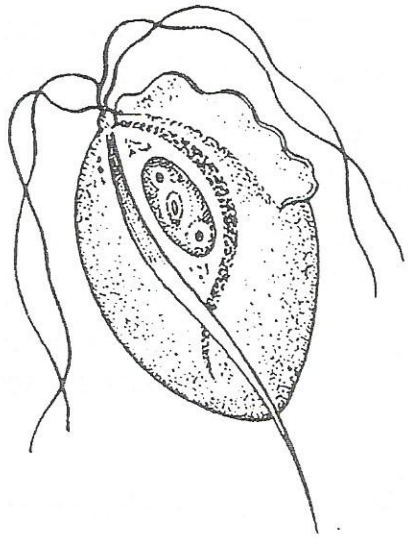
▸ TREATMENT ………*CDC recommendation*……….

Flagyl = Metronidazole ¤ (500 mg 1x2x7)……….or……..local gel
Clindamycin –dalacin C– (300 mg 1x2x7)……….or…….local cream
Broad spectrum as erythromycin, tetracycline ……500 mg 1x4x7…✗



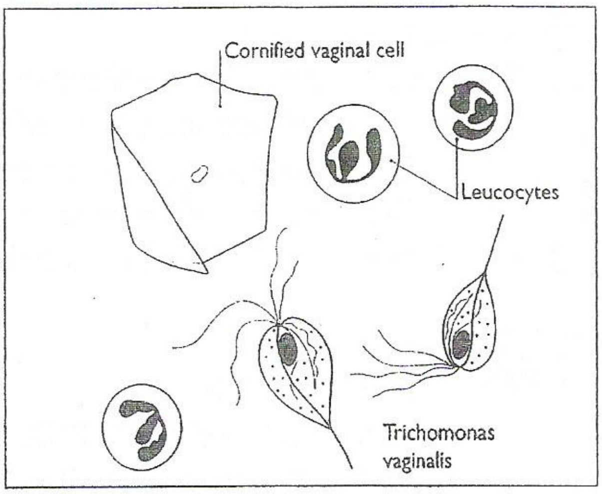
Mycelia and spores of C.albicans. Note the presence of leucocytes.

TRICHOMONAS VAGINALIS



KEY POINTS

1. As with vulvitis, the number one cause of vaginitis is *Candida*.
2. Diagnosis is often made with a wet prep (trich and BV) or KOH prep (yeast).
3. In the absence of microscopic evidence, symptoms and type of discharge should dictate the treatment.

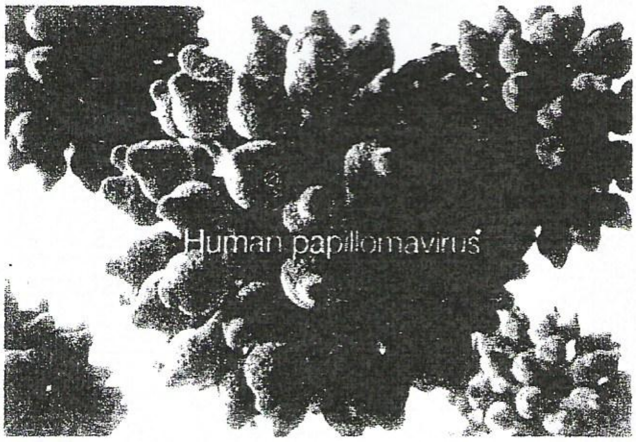


Trichomonas vaginalis.

KEY POINTS

1. Seventy-five percent of sexual partners of those with *Trichomonas* will also be colonized and should be presumptively treated.
2. Diagnosis is made via wet prep, but is usually presumed with a profuse, malodorous, gray-green, frothy discharge.
3. Treatment is metronidazole 2 g orally one time.

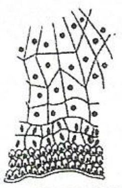
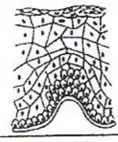
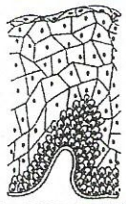
⚜	❹ candida (monilia, thrush) 2nd cause of V.vaginitis (30%)	❺ trichomonas vaginalis 3rd cause of V.vaginitis (25%)
Predisposing factors ¤¤	- ↑ vaginal acidity & moisture - ↑ vaginal epithelial glycogen (pregnancy / COC pills)	- Alkaline medium
	- ↓ resistance (DM, steroids) - Prolonged use of antibiotics (altered flora balance)	
Mode of infection	. NORMALLY present in vagina (20-40% candida)…(50% TV) . Contamination from → STD✓✓, hands, towels, instruments	
Clinical Picture	- Premenstrual - Severe vulvovaginitis (PPdd) - Discharge is ODORLESS, whitish thick, curdy-cheese like, scanty O/E → adherent white patches → removal leaves slight bleeding	- Postmenstrual - Severe vulvovaginitis (PPdd) - Discharge → MALODOROUS, greenish, frothy, profuse O/E → red edematous +punctate hge (STRAWBERRY vagina ¤)
Investigation	▫ PH → *acidic* ¤ ▫ Smear → Gram +ve ▫ Fresh *drop of discharge* → hyphae or mycelia ▫ Culture medium Sabouraud's ¤ / Nickerson ▫ Antigen detection → microstix	▫ *alkaline* ▫ G –ve ▫ motile flagellated organism (slightly larger than leucocyte) ▫ Diamond, Feinberg, Trichocele ▫ Colposcopy: T-shaped vessel
- Prophylaxis	Eliminate pdf + use alkaline /	acidic vaginal douches
- Treatment	* Local - Mycostatin (Nystatin) - Clotrimazole (Canestan) - Miconazole (Daktarin) * Oral (in virgins, resistance) - *Ketoconazole* (Nizoral) 200 mg 1x2x5 - *Fluconazol* (Diflucan) 150 mg once - *Itraconazole* (Sporanox) 1gm once	* Local - Metronidazole vag tab. (500 mg ¤) 1x1x10 * Oral - *Metronidazole* (500 mg) 1x2x7 - *Tinidazole* (better compliance) (2 gm once) 4 tablets - *Ornidazole* (1.5 gm once) 3 tablets
- Recurrence	. Treat pdf (e.g. DM) . Extend ttt for 3-6 weeks	/ TREAT HUSBAND (in all inf) ✓✓ / Avoid vaginal douches



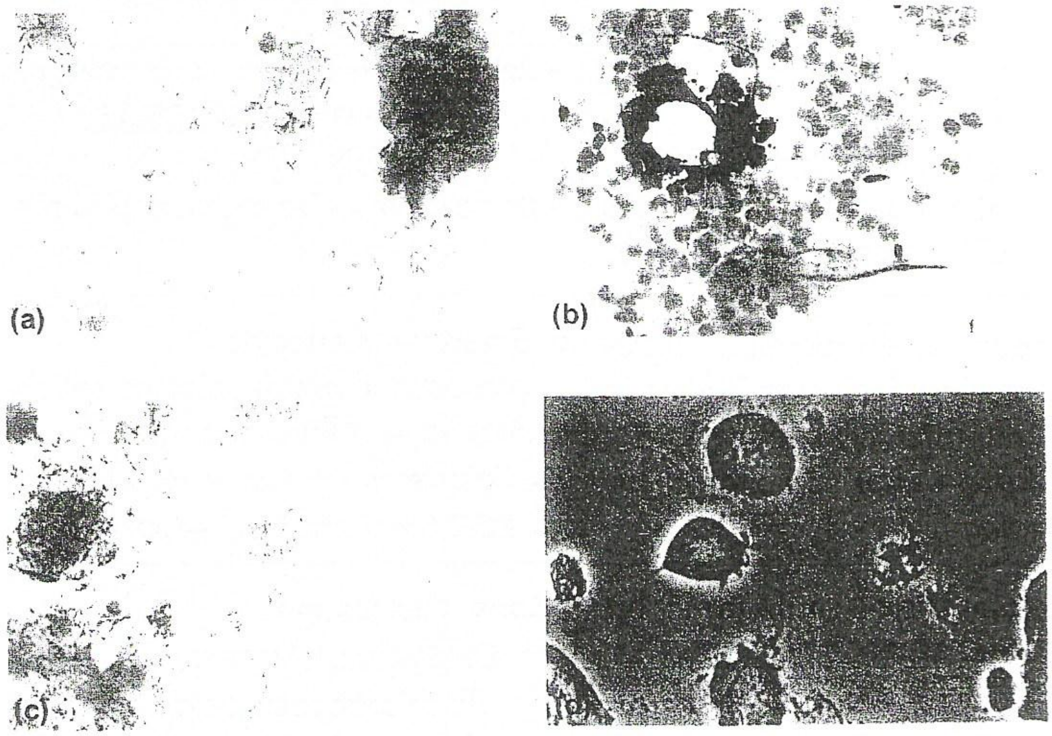
KEY POINTS: genital warts

- Most genital warts are caused by sexually transmitted strains of HPV.
- Long-lasting resolution of visible warts requires a good cell-mediated immune response.
- Infections persist for many years, and relapse can occur at any time.
- Several types of HPV, particularly 16 and 18, are associated with cervical cancer.
- Attention should be paid to reversible risk factors such as smoking.

⚜	❻ Herpes simplex	❼ Human Papilloma virus
Virology	* usually type **II** ↘ sometimes 20% type **I** ¤ - DNA virus ¤ - Incubation period → 5–7 days - May affect → vulva, perineum, vagina, cx, urethra, oral cavity	* Papova virus family (genital warts) ↘ the commonest ✓ viral STD ¤ - DNA virus ¤ - 70 sero-types (**6,11**.....16,18.....31,33,35,39 ......41,43,44....51,52,56)
Clinical picture	* <u>Primary</u> (1st infection) . General ⇨ FAHM (flu-like) . Locally ⇨ painful vesicles → shallow grey ulcers + LN . Fate ⇨ heals rapidly spont. but remains dormant in sacral ganglia * <u>Secondary</u> (reactivation) . General symptoms → none . Local → mild sympt ¤ + no LN	* <u>Types</u> . Condyloma accuminatum ↘ on vulva, anus, perineum ↘ multiple cauliflower masses . Flat condyloma ¤ ↘ especially on cervix . Inverted condyloma * <u>Recurrence</u> (60%) esp in ⇨ . Pregnancy, COC . DM, immunosuppression
Comp's	- **Secondary infection** - **Urinary retention** ¤ - **On pregnancy** → abortion, PTL - **On newborn** → encephalomyelitis (∴ CS if having *active* HSV)	- **Related to malignant & premalignant** lesions of LGT (**16,18**) ¤ e.g. CIN, VIN, VAIN - **On newborn** → laryngeal papilloma
Inv's	▫ *Smear* → eosinophilic intra-nuclear inclusion bodies in multinucleated giant cells ▫ *Culture* → chorioallantoic memb ▫ *Serology* → CFT, IFT	▫ *Smear* → Koilocytes ¤ (vacuolated multinucleated cells) ▫ *Biopsy* → mimics malig. ∴ *Colposcopy* + *Pap* → exclude malig ∴ *PCR Southern blot* ¤ → specific type
TTT	- **Symptomatic** ± antib. for 2^{ry} inf. - **Antiviral drugs** ↘ doesn't eradicate it but ↓ convalescence & recurrence ¤ . Acyclovir, idoxuridine (1x5x5) → most used . New oral drugs (famciclovir, valacyclovir) → 1x2x5 . Interferon & specific vaccines	- **Local destruction** * CHEMICAL CAUTERY .Trichloroacetic acid ¤ 75% .Podophyllin resin 0.5% → toxic .Imiquimod 5% → self applied * CO_2 LASER, CRYOCAUTERY - **Surgical excision** - **Antiviral agent as** 5% 5-fluorouracil - **Vaccination** (2006 in USA) ✓✓✓✓

	Vaginal				
	Oestrogen	Epithelium	Glycogen	pH	Flora
New born	+		+	Acid 4–5	Sterile ↓ Doderlein's bacilli Secretion abundant
Month-old child	–		+	Alkaline >7	Sparse, coccal and varied flora. Secretion scant
Puberty	Appears		– → +	Alkaline ↓ Acid	Sparse, coccal ↓ Rich bacillary
Mature	+ +		+	Acid 4–5	Doderlein's bacilli Secretion abundant
Post menopause	+ → –		–	Neutral or alkaline 6 to >7	Varied Dependent on level of circulating oestrogen Secretion scant

Cyclic changes in the vagina related to age.



(a) Normal: lactobacilli
(b) Candidiasis:
(c) Bacterial vaginosis.
(d) Trichomoniasis:

Vulvovaginitis ✍

➡ Primary (1^{ry})

Bacteria → Ğ, **Bacterial vaginosis** ❶,......................Š, Ťß
Fungal → **Candidiasis** ❷
Parasites → **Trichomonas vaginalis** ❸,......................ß
Chlamydia → lymphogranuloma venereum (LGV)
Viruses → HSV, CMV, HPV (cond. accuminatum)

➡ Secondary (To)

- ▶ **Cervical & vaginal discharge**
- ▶ **Urinary conditions** → incontinence, fistula, glucosuria, pyuria
- ▶ **Rectal conditions** → R-V fistula, complete perineal tear
- ▷ *Chemical* → douches, sprays, perfumes
- ▷ *Physical* → scratching, irradiation
- ▷ *Traumatic* → foreign body, prolapse, neglected pessary

Clinical picture

.Symptoms → - **P**ain (soreness) & **P**ruritis vulvae
- **D**ysuria & **D**yspareunia
- **D**ischarge............<u>mention the discharge of</u> ❶ ❷ ❸

.Signs → red, hot, swollen, edematous, tender
± inguinal lymphadenitis ± scratch ulcer

Investigations

. Any discharge → bacteriological examination.....<u>mention the inv. of</u> ❶ ❷ ❸
. Any suspicious area → skin biopsy e.g. from leucoplakia........esp. in old age
. Any suspicion of DM (severe itching ± moniliasis)...............esp if recurrent

Treatment

1] **<u>Of cause</u>**.................... <u>mention the ttt of</u> ❶ ❷ ❸
2] **<u>Local</u>**
- Good local hygiene ⇨ . keep vulva dry & clean (best is neutral douche)
. Underwears should be *cotton, loose, dry*
- Antipruritic ⇨ antihistaminic ± anesthetic ± cortisone

3] **<u>General measures to ↓ irritation</u>**
- Sedatives → phenobarbitone
- Antihistaminics

☞ Bartholinitis

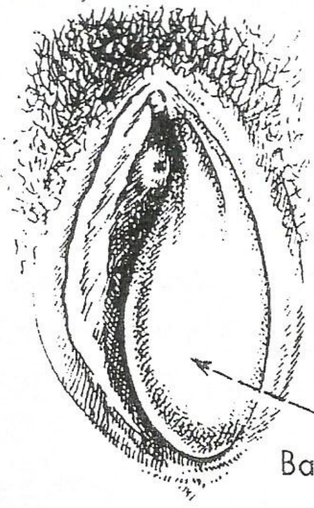
Pathology: acute inflammation of Bartholin gland (E.coli ¤)

C/P *Symptoms* → pain: 1st aching then throbbing (if pus forms)

Signs → . Red edematous skin + induration
. Pus may be discharged from the duct
. Gland is palpable & tender

Fate ⇨ complete resolution.....abscess formation
.....*chronic bartholinitis* ✓

TTT - Bartholinitis → antibiotics + hot fomentation
- Bartholin abscess → incise & drainage



☞ Bartholin cyst

Pathology

- It is the commonest VULVAL cyst ✓ ¤
- Due to obstruction of the gland duct by → infection, mucous, *trauma*

Types

- *Cyst of the duct* is much more common ✓ (lined by transitional epithelium)
- *Cyst of the gland* is rare (lined by columnar epithelium)

C/P ⇨ painless cystic swelling in the lower ⅓ of the labia majora

TTT

1. **Marsupialization** ✓ ¤
- Elliptical incision of the cyst & suturing the edges to the surrounding
- Advantages → preservation of the lubricant function, less bleeding

2. **Excision** (esp. postmenopausal d.t. risk of hidden...............)

☞ Toxic shock syndrome

Path. → Tampon use → introduction of Staph. Aureus ¤ → multiplication in retained menstrual blood in tampon → exotoxin → systemic effects

C/P (after 2nd day of menses)
- FAHMR
- Septicemia → hypotension, diarrhea, skin edema
- Organ affection → liver, kidney, heart, DIC

TTT . Resuscitation in ICU
. Remove tampon
. Antibiotics according to C&S from vagina & tampon

☞ Prepubertal (childhood) Vulvo-vaginitis ✍

PDF ⇨ thin vaginal mucosa (d.t. ↓ estrogen → ↓ vaginal acidity)

Mode of infection

❶ *Primary*

- * Congenital → cong. fistula, ectopic anus......**parasites** (oxyuris, amoebiasis)
- * Inflammatory → transmission from adult ...**STD** (Ğ, TV, monilia)
- * Traumatic → accidental FB in vagina ✓......**non-specific** (staph, str., E.coli)
- * Neoplastic → sarcoma botryoids

❷ *Secondary*

- * Chemical irritation → diaper rash, soaps
- * Poor hygiene → wiping perineum from anus to vagina

C/P ⇨ . as vulvitis & vaginitis ♒ ♒
. Note presence of lacerations (*trauma*), peri-anal erythema (*parasites*)

TTT

.GENERAL INSTRUCTIONS → antihistaminics, antipruritics, local hygiene
.TREATMENT OF THE CAUSE → any discharge → smear, gram stain
antibiotic is given according to C&S
.IN RESISTANT CASES → may give 'E' ?? locally to increase resistance
.IF PERSISTENT/SEROSANGINOUS DISCHARGE → inspect for F.B. / tumors:
➡ P/R, X-ray, U/S, vaginoscope (or cystoscope)

☞ Senile (atrophic) Vulvo-vaginitis

PDF ⇨ thin vaginal mucosa (d.t. ↓ 'E' → ↓ vaginal acidity) → mixed inf.

C/P ⇨ postmenopausal scanty yellowish / serosanginous discharge + PPdd

TTT

.GENERAL INSTRUCTIONS → antihistaminics, antipruritics, local hygiene
.TREATMENT OF THE CAUSE → any discharge → smear, gram stain
antibiotic is given according to C&S
. IN RESISTANT CASES → 'E' locally (premarin) or orally (0.625mg) for few wks
. IF PERSISTENT / SEROSANGINOUS DISCHARGE → D&C to exclude
➡ endometrial carcinoma or associated senile endometritis

Cervicitis

1) Acute cervicitis

Causative organisms

. Non-specific → strept., staph., E.coli
. STD's → monilia–**TV**,.........viruses..........., **Ğ–chlamydia**

Route → *Obst* (abortion, labor)..........*Gyn* ($D_{\&}C$ /IUCD, intercourse)

Clinical picture

Symptoms - General → FAHM-R
- Local → discharge, dyspareunia, BACK PAIN

Signs
. Red, swollen, tender on mobility,
. exuding mucopurulent or purulent discharge

Treatment ⇨ antibiotics systemically + antiseptic pessaries

2) Chronic cervicitis

Causative organisms

. Non-specific......STD's....chronic granulomatous (Ťß, ß, actinomycosis)
. Either ↷
* **Persistence of acute cervicitis → chronic** (due to:)
- Glands are racemose → difficult drainage
- No monthly shedding of epithelium
- The glands are in the depth so if surrounded by fibrosis → difficult penetration of antibiotics

* Chronic from the start as → postoperative, postabortive, postpartum infected lacerations

Pathological forms

1. **Chronic endocervicitis** ⇨ normal cx exuding mucopurulent discharge
2. **Mucous polyp** ⇨ hyperplasia of endocx epith.→ multiple small reddish polyps
3. **Nabothian follicles** ✓✓⇨ obstruction of gland ducts → multiple small retention cysts either: *bluish* (full of mucus) or *yellowish* (pus)
4. **Chronic hypertrophic cervicitis** ⇨ swelling & hyperemia of cx
5. **Chronic atrophic cervicitis** ⇨ cervical stenosis
6. **Cervical ulcers** ⇨ bright red erosions (true ulcers)
7. **Ectropion** ⇨ eversion of the endocervical mucosa (d.t. bilateral cx tears)

Clinical picture (it affects many women.....mostly is asymptomatic)

☆ **Symptoms.....congestive symptoms**

- Discharge → mucopurulent or purulent
- Pain → - **D**ysmenorrhea (congestive)
  - **D**yspareunia
  - **D**eep lower abdominal pain (affection of parametrium)
  - **D**orsal pain (affection of uterosacral ligaments)
- Bleeding → contact bleeding

☆ **Signs............tenderness on movement + any pathological form**

Complications

- Pregnancy → abortion, PROM, infection
- Gynecology
  - ↘ Spread → . local: to vulva (PPdd), UTI (frequency, dysuria)
    . General: acts as aseptic focus → rheumatic pains
  - ↘ Infertility → hostile cervical mucus
  - ↘ Malignancy (after HPV)

Investigations

C.ulture → swab from endocervix for gonorrhea or chlamydia

B.lood → ↑ ESR, TLC, CRP

C.omplications

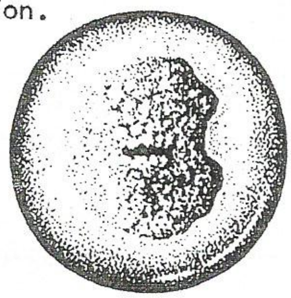
- *Colposcopy* → to exclude malignant conditions
- *Infertility* → post coital test

Treatment

1. ***Prophylaxis***
   - Avoid sexual promiscuity
   - Aseptic techniques (delivery, D&C, IUCD)
   - Prompt diagnosis & early ttt......otherwise....chronic cervicitis
2. ***Medical***
   - Warm vaginal douches
   - Antiseptic pessaries e.g. albothyl ✓
   - Antibiotics → not effective (deep seated infection)
3. ***Cauterization*** ⇨ electrocautery, cryocautery, chemical, Laser
4. ***Surgery***
   - Conization
   - Amputation
   - Rarely hysterectomy (extensive infection or if coexisting disease)

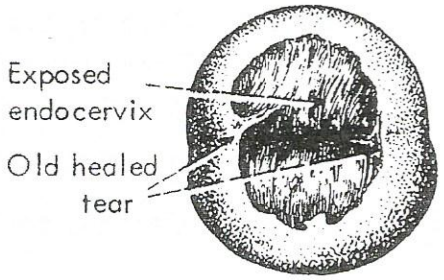
CERVICITIS

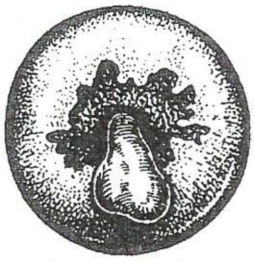
An infection of the cervical epithelium and stroma, usually following erosion.



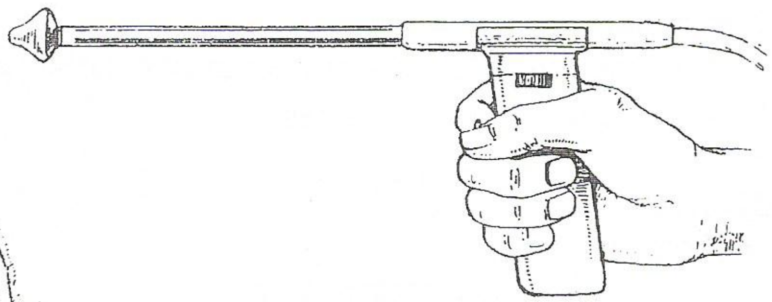
ECTROPION

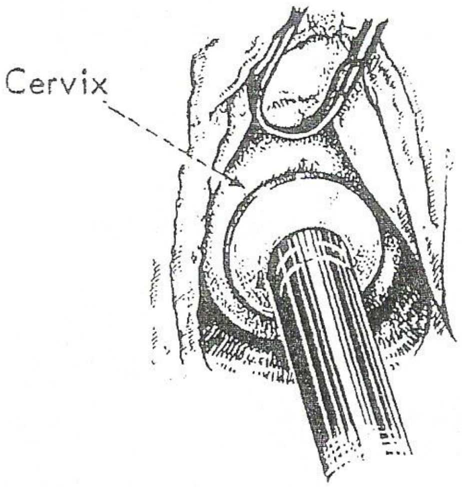
An erosion or infection in a gaping or lacerated cervix.





Cervical polyp
with cervicitis





Diathermy under general anaesthesia will destroy tissue to a depth of 7-8mm.

Differential diagnosis

1. ***Causes of cervicitis***

2. ***Causes of leucorrhea & vaginal discharge***

3. ***Causes of contact bleeding***

Definition ⇨ bleeding after intercourse, vaginal examination, douching

Etiology ⇨ . Cervicitis / cervical erosions / cervical ulcers
. CIN / Cancer cervix
. Vaginal or uterine tumors bulging into vagina
. Severe vaginitis esp senile type

TTT ⇨ smear & colposcopy → specific management

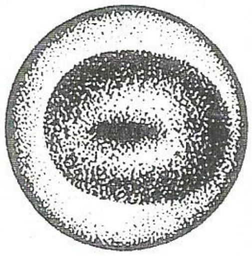
4. ***Causes of cervical Ectopy (Erosion)*** ✍

Definition: . Replacement of columnar epith. to the normal squamous lining of part of ectocervix → shows underlying vessels
. Erosion is not an accurate name (as it usually said instead of ulcers ¤ – denuded epithelium)

Etiology
- Chronic cervicitis
- Congenital → persistence of columnar lining of ectocervix (normally present intrauterine only)
- Hormonal → ↑ 'E' as in → pregnancy, lactation, COC

Symptoms (*asymptomatic*)
- Mucoid vag discharge (purulent if infected)
- Contact bleeding (rare)

Signs
a) *Simple* (flat) → bright red area at ectocervix
b) *Papillary* → velvety appearance
c) *Follicular* → blue or yellow



Simple erosion

Investigation ⇨ *smear*, *colposcopy*, *biopsy* to exclude CIN

TTT
⇨ According to cause: *hormonal* (follow up)....*cervicitis* (antibiotics)
⇨ if failed: **CAUTERIZATION** but avoid 3, 9 o'clock

* *Electrocautery* ⇨ coagulates unhealthy tissue + drainage of deep glands

* *Cryocautery* ⇨ using CO_2 or N_2 at -60°c for 2-4 minutes
. Disadv → profuse watery discharge (very common)

* *Chemical cautery* ⇨ $AgNo_3$ or conc. $ZnCl_2$ using Fergusson speculum

* *Laser therapy* ⇨ rapid healing with minimal fibrosis, less side effects

Endometritis

TYPES

Acute	Chronic
Puerperal sepsis	Non-specific ⇨ rare due to cyclic shedding
Postabortive	Specific ⇨ bilharziasis, **T.B.**, actinomycosis

CLINICAL PICTURE → irregular cycles, amen., infertility, dysmen., discharge

Pyometra

Definition → pus in the uterus

Etiology → infections + obstruction by

- Cancer (cervix, endometrium)
- Stenosis (post ➠ menopausal, cauterization, irradiation)

Clinical picture

Symptoms: . General → FAHM-R
. Abdominal → lower abdominal pain
. Vaginal → intermittent purulent discharge

Signs: . Enlarged tender uterus
. SOUNDING → pus from cervix

Treatment

- Drainage by DILATATION then antibiotics
- Curettage after 2 weeks for diagnosis of possible tumors

Parametritis

Definition → inflammation of the CT within the leaflets of broad ligament

Etiology → direct or lymphatic spread from

- Cervicitis / endometritis after abortion or labor / salpingoophritis
- Genital tract malignancy (d.t. infection or radiotherapy)

Pathology

. Inflammatory collection in the broad ligament
. Fate → resolution / chronicity / abscess formation

Clinical picture

- Sympt. → FAHMR + lower abdominal pain + sympt of p.congestion
- Signs → tender swelling pushing the uterus to the opposite side

Treatment → as pelvic abscess

Pelvic inflammatory disease

DEFINITION

Infection & inflammation of upper genital tract i.e.
Tubes, ovaries, pelvic peritoneum (± uterus) ⇨ 2-3% of population

ETIOLOGY

PDF

- *Sexually active females* with multiple sexual partners....usually after menses (loss of cx plug, degenerated endomet, retrograde menstruation)
- *IUCD users* (Barriers + COC → ↓ PID)
- *Recent instrumentation* of uterus (e.g. D&C / HSG)

Routes of infection

- *Ascending* through
  - . LUMEN (as chlamydial & gonococcal) ⇨ *endosalpingitis*
  - . LYMPHATICS (esp puerperal & postabortive) ⇨ *interstitial salpingitis*
- *Direct* from neighboring organs as appendicitis ⇨ *perisalpingitis*
- *Blood* spread as T.B.

❶ Acute PID

Etiology

- STD's esp GONOCOCCUS (40%), CHLAMYDIA✓ (60%¤)
- Puerperal or postabortive
- Non-specific organisms (aerobic or anaerobic) :usually mixed

Pathology

a) **Acute catarrhal salpingitis**

- Resistance of the patient is high
- Infection only of m.m. → serous exudate in lumen
- Fate → complete resolution

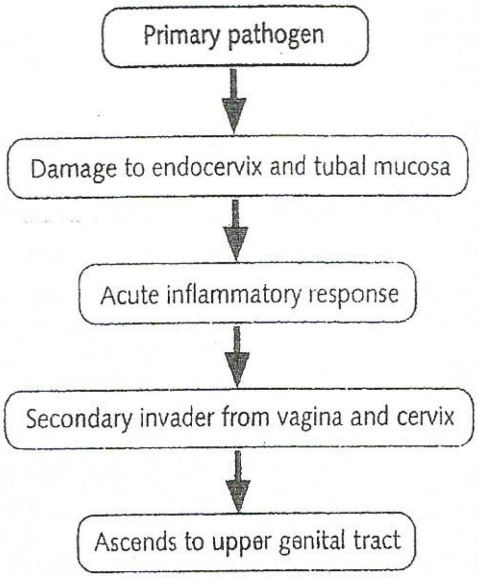
b) **Acute suppurative salpingitis**

- Virulence of the organism is high
- Infection extends to all layers → purulent exudate in lumen
- Fate → chronicity, spread (pelvic peritonitis)

c) **Acute perisalpingitis** ⇨ fimbrial adhesions → closure of fimbrial end

PID risk factors

Risk factor	Description
Age	75% of patients are below 25 years of age
Marital status	Single
Sexual history	Young at first intercourse High frequency of sexual intercourse Multiple sexual partners
Medical history	Past history of sexually transmitted disease in patient or partner Past history of PID in patient Recent instrumentation of uterus, e.g. termination of pregnancy
Contraception	Use of IUD especially insertion within 3 weeks



Development of PID.

Complications of acute PID

Type of complication	Description
Short term	Pelvic abscess formation Septicemia Septic shock
Long term	Infertility Ectopic pregnancy Chronic pelvic pain Dyspareunia Menstrual disturbances Psychological effects

KEY POINTS

1. There may be as many as 1 million cases of PID reported annually.
2. Twenty percent of patients with PID will become infertile.
3. PID can be diagnosed with uterine and adnexal tenderness, fever, elevated WBC count, and cultures or tests for gonorrhea and *Chlamydia*.
4. Because of the seriousness of this disease and its sequelae, patients are often hospitalized and treated with IV antibiotics.

KEY POINTS

1. Chronic or acute PID can lead to TOAs or TOCs.
2. Diagnosis of TOA or TOC is most likely when there is an adnexal mass in the setting of PID symptoms. Confirmation is usually achieved with an imaging study such as pelvic ultrasound or CT.
3. Treatment includes hospitalization and IV antibiotics. For TOAs not responsive to antibiotics, adnexal surgery is the definitive cure.

Clinical picture

1. **Symptoms (history of pdf +)**
   - General → FAHM-R
   - Abdominal → acute lower abdominal pain
   - Pelvic → congestive symptoms (pain, bleeding, discharge) 🗝
2. **Signs**
   - General → signs of infection
   - Abdominal → . tenderness & rigidity in lower abdomen (peritonitis)
     . maximum 3 cm above mid-inguinal point (tubal point)
   - P/V → tender movement of cx, tender adenexae ± tender mass

	N. gonorrhea (worser)	C. trachomatis
Onset	More acute Usually after menses	May remain for months in tube
C/P	Acute pain ± peritonitis	Milder (silent PID)
Comp.	Diffuse exudate → tubal block	More damage but later on

Investigations

C.ulture → swab from endocervix, rectum, pharynx
B.lood → ↑ ESR, TLC, CRP
C.omplications
- **Ultrasound** → adnexal swelling
- 🗝 **Laparoscopy** → . red, swollen, edematous tube ± mass
  ↳ (gold standard) . Pus may exude from fimbrial end → cytology

Criteria for diagnosis

Minimum criteria	+ One additional
- Lower abd. pain ±T ± RT - Adenexal tenderness - Cx motion tenderness	- Temp > 38°c, ↑ ESR, TLC > 10.500 - Inflammatory mass (by P/V or U/S) - Org. ±pus (lap., culdocentesis, endocx swab)

Differential diagnosis ⇨ ....causes of acute abdomen........

- Disturbed ectopic, acute appendicitis
- Ruptured ovarian cyst, complicated fibroid
- Inflammatory bowel disease e.g. appendicitis, diverticulitis

Complications

- Recurrence.........Chronicity –esp chlamydia– (chronic pelvic pain)
- **Infertility**............**Ectopic** pregnancy
- Spread →........- Pelvic abscess formation
  - Thrombophlebitis
  - Peritonitis, Septicemia

CDC RECOMMENDATION FOR PID

<table>
<tr><th colspan="3">Parenteral</th><th></th><th colspan="3">Oral</th><th></th></tr>
<tr><td>Cefoxitin
2 g IV / 6hr</td><td>or</td><td>Cefotetan
2 g IV / 12 hr</td><td rowspan="5">A</td><td colspan="3" rowspan="2">Levofloxacin 500 mg
1x1x14</td><td rowspan="2"></td></tr>
<tr><td colspan="3">+ doxycycline 100 mg IV / 12hrs</td></tr>
<tr><td colspan="3">OR</td><td colspan="3">OR</td><td></td></tr>
<tr><td colspan="3">Ampicillin/sulbactam 3g IV/6 hr
+ doxycycline 100 mg IV / 12hrs</td><td colspan="3">Ofloxacin 400 mg
↙ Plus ↘</td><td rowspan="2">1x2X14</td></tr>
<tr><td colspan="3"></td><td colspan="3">Doxycycline 100
Metronidazole 500</td></tr>
<tr><td rowspan="2">Clindamycin
900 mg
IV /8 hr</td><td rowspan="2">PLUS</td><td rowspan="2">Gentamycin
Loading
2 mg/kg
→ 1.5 mg/
kg/8 hr</td><td rowspan="2">B</td><td colspan="3">↖Plus ↗</td><td rowspan="2"></td></tr>
<tr><td>Ceftriaxone
250 mg
once</td><td>OR</td><td>Cefoxitin
2 gm
once</td></tr>
</table>

NB.....antibiotics in pregnancy

- The most safe are *penicillins / cephalosporins*
- *Anti-tuberculous* drugs could be given
- *Quinolones* are absolutely contraindicated
- Intravaginal *antifungals* (candida) are safe from first trimester
- *Metronidazole* (Trichomonas) can be used in 2nd & 3rd trimester

Treatment

Prophylaxis

- Avoid sexual promiscuity
- Aseptic techniques (delivery, D&C, IUCD)
- Prompt diagnosis & early ttt……otherwise….chronic PID within ……

Active

General lines

- Antipyretics
- Analgesics & hot fomentation
- Antibiotics in combination in high doses
- Complete bed rest in Fowler position
- Treatment of partners

Indications for hospitalization

- Nulliparity or low parity → to avoid infertility
- Bad general condition
    - Large mass (tubo-ovarian complex felt on P/V)
    - Complicated mass (ruptured tubo-ovarian mass)

Antibiotic therapy **(continued 48 hrs after resolution of fever)**

- Regimen I……..cefoxitin (2nd) or cefotaxime (3rd) + Doxycycline
- Regimen II……clindamycin + gentamycin
- Regimen III…..ampicillin + gentamycin + metronidazole

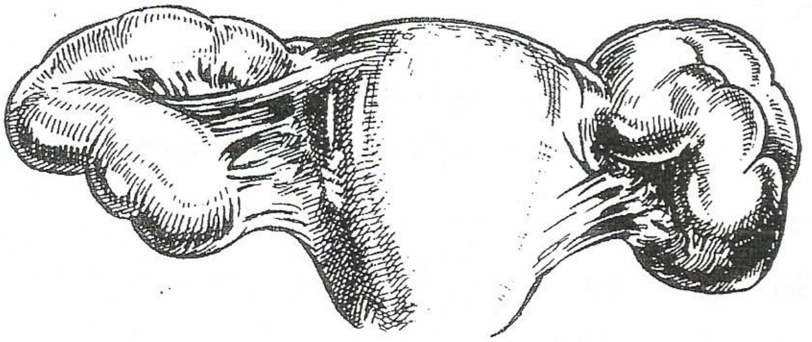
NB…. CDC recommendation for PID

NB…. TTT of specific organisms (uncomplicated)

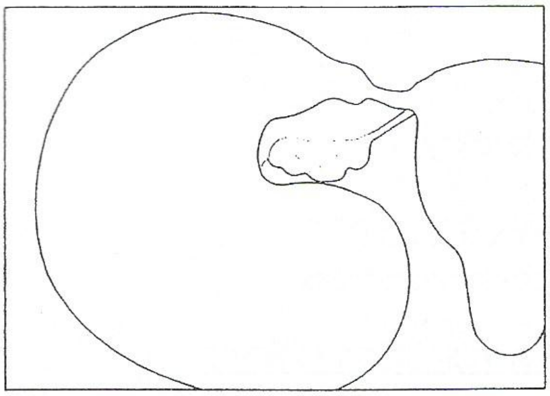
- GONORRHEA single dose of *ceftriaxone* 250 mg (IM) or *cefixime* 400 mg, *ciprofloxacin* 500 mg (oral)
- CHLAMYDIA (a usual association) → azythromycin 1gm

Surgical intervention

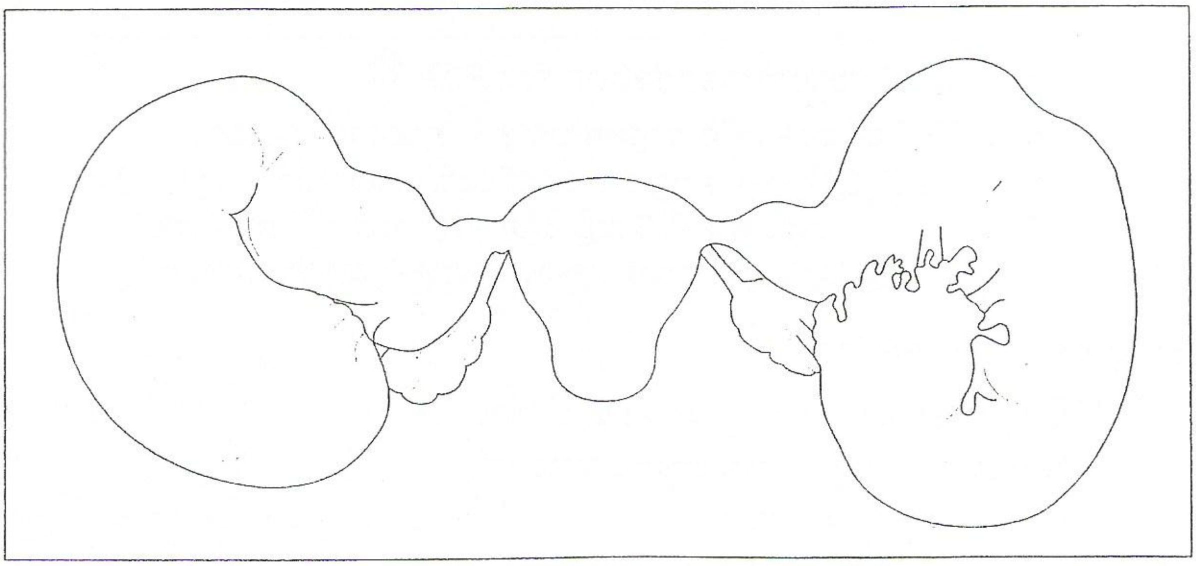
- *If* ❶ *severe disease refractory to medical ttt or*
  ❷ *ruptured / huge tuboovarian abscess or*
  ❸ *generalized peritonitis*
  ↘ *Laparotomy ✓✓ + drainage + peritoneal toilet*
  ± ……. unilateral adenexectomy (to preserve fertility)
  OR ……pelvic clearance = TAH +BSO (for older age)
- *If small tuboovarian abscess* → aspiration ✗ (U/S guided or Laparoscopy)
- *Pelvic abscess* → drain by posterior colpotomy
- *Thrombophlebitis* → heparin



Blocked and distended tubes in PID



Hydrosalpinx. Note the retort-shaped distension of the oviduct.



Bilateral chronic salpingitis.

❷ Chronic PID ✍

Etiology

. STD's……non-specific….chronic granulomatous (ŤB, B)

. Either ↷

* **Persistence of acute PID** (due to:)
    - Glands are racemose → difficult drainage
    - The glands are in the depth so if surrounded by fibrosis → difficult penetration of antibiotics

* **Chronic from the start**

Pathology

1) **Hydrosalpinx**
   - Catarrhal salpingitis → closure of the fimbrial end → distension with serous fluid → pelvic pressure ± pain
   - HSG → retort shaped swelling
   - It is liable to → torsion, infection, rupture

*Tuboovarian cyst ⇨ hydrosalpinx communicating with ovarian cyst

2) **Pyosalpinx**
   - Suppurative salpingitis → thickened tube full of pus
   - HSG → smaller in size than hydrosalpinx
   - Less liable for torsion than hydrosalpinx (infection → adhesions)

*Tuboovarian abscess ⇨ pyosalpinx communicating with ovarian abscess

3) **Perisalpingitis**
   - Thickened, kinked tube surrounded by adhesions → infertility, ectopic

4) **Salpingitis isthmica nodosa** (chronic interstitial salpingitis)
   - Multiple bilateral nodules & diverticula (esp in isthmus)
   - DD → TB, B, gonococcal, endometriosis (± m.b. in healthy tubes?)

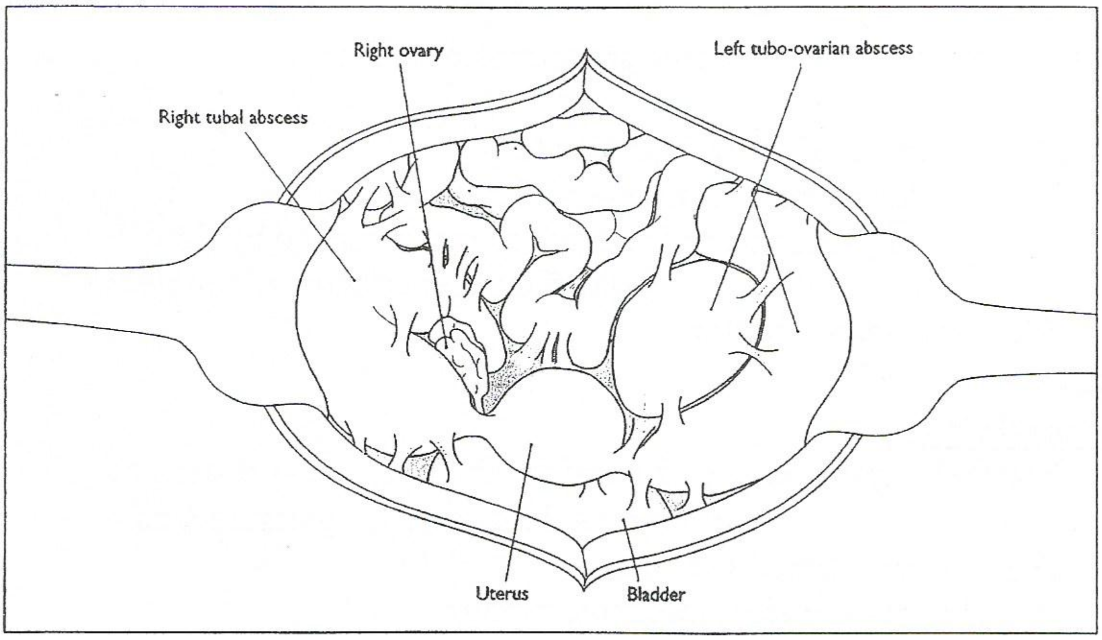
5) **Fitz-Hugh-Curtis syndrome**
   - Perihepatitis associated with chronic PID (esp chlamydia, gonorrhea)
   - C/P → recurrent upper right abdominal pain (DD: cholecystitis)
   - Inv. → laparoscopy → violin string-like bands of adhesions

Clinical picture

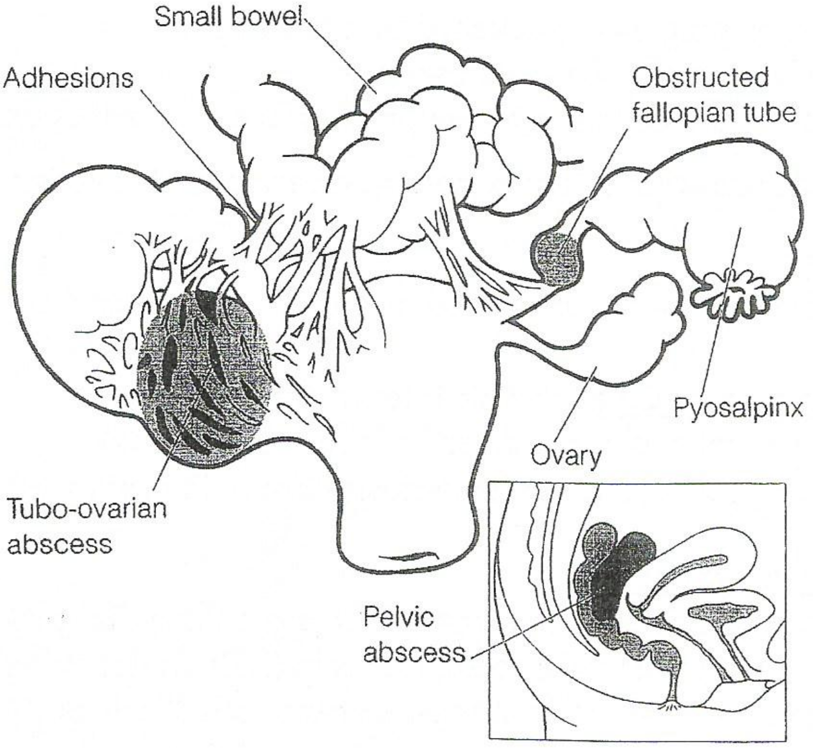
▸ History → previous attacks of acute PID or ectopic

▸ Symptoms

- Infertility
- Congestive symptoms ⊶
- Recurrent acute exacerbations



Bilateral pyosalpingitis – the appearance at operation.



• Findings associated with chronic pelvic inflammatory disease, including tubo-ovarian abscess, adhesions, pyosalpinx, and an abscess located in the posterior cul-de-sac.

▸ **Signs**
- General → ill health....TB toxemia
- Abdominal → signs of TB peritonitis or bilharziasis HSM
- Pelvic → . Tenderness (lower abdominal, cervical motion) ✓
  . Tubo-ovarian (adenexal) mass ✓✓
  . Fixed RVF

Differential diagnosis .........ENDOMETRIOSIS, CANCER OVARY, TB

Investigations

- *Diagnosis* ⇨
  - **C.ulture** → swab from endocx, rectum, pharynx (chlamydia, gonorrhea)
  - **B.lood** → ↑ ESR, TLC, CRP
  - **C.omplications**
    - **.Ultrasound**.......if pain prevents PV & to follow up TO abscess size
    - **.Laparoscopy**....if diagnosis is uncertain or no improvement within 48-72 hr
- *Etiology* ⇨ TB (tuberculin, chest X-ray)
- *Comp.* ⇨ e.g. infertility → HSG, laparoscopy (± tubal biopsy)

Treatment

Prophylactic → prevent puerperal, postabortive & surgical infection

Active
- *Acute exacerbations* → medical ttt for 48 hours initially
  . Rest, fluids, Fowler position
  . Antibiotics, hot fomentation
- *If good response* (improvement of general health) → continue
- *If no response* or *there is a mass (abscess) from the start* → surgery
  . Unilateral adnexectomy (if young → conservative)
  . TAH + BSO (esp if bilateral & > 40 years)
  . If infertility → tuboplasty fails ∴ remove + IVF/ICSI (better)
- *In chronic specific* → treat cause as B or TB

Pelvic abscess ☞

Etiology

1^{ry} → not preceded by *pregnancy / trauma / surgery* → better prognosis
2^{ry} → postabortive, postarptum, post-ectopic (infected haematocoele)
post-traumatic, extension from near by focus (appendicitis)

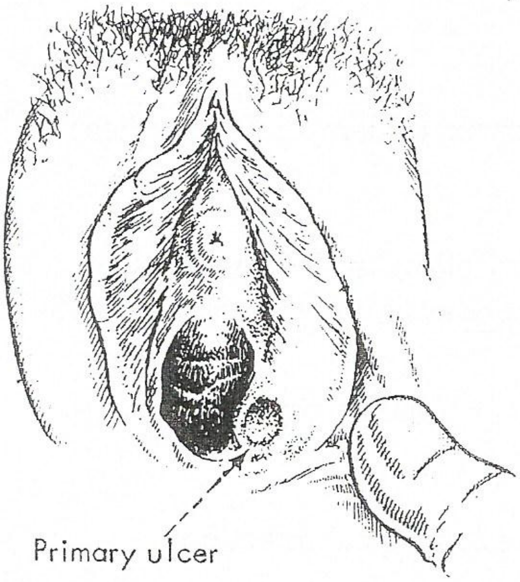
Organisms → usually mixed (1^{st} aerobes then anaerobes)

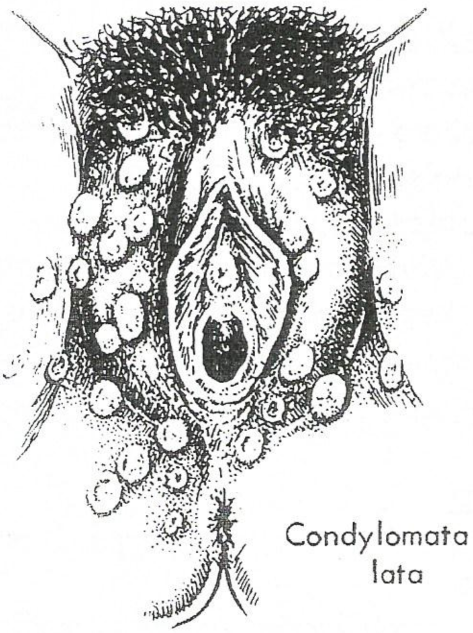
Clinical picture

Symptoms → ⊶ (pain more severe) ± urinary & rectal pressure symptoms

Signs - Tender cervix, tender adenexae
- Tender soft swelling in Douglas pouch (also felt by PR)

Treatment → as in chronic PID





Infectious Causes of Ulcerated Lesions

	Syphilis	Herpes	Chancroid	LGV
Incubation period	7–14 days	2–10 days	4–7 days	3–12 days
Primary lesion	Papule	Vesicle	Papule/pustule	Papule/vesicle
Number of lesions	Single	Multiple	1–3, occasionally more	Single
Size	5–15 mm	1–3 mm	2–20 mm	2–10 mm
Painful	No	Yes	Yes	No
Diagnostic test	Dark-field microscopy RPR/MHA-TP/FTA-ABS	Viral culture	Gram's stain with "school of fish" appearance	Complement fixation
Treatment	Penicillin	Acyclovir	Ceftriaxone or azithromycin	Doxycycline

Chronic granulomatous diseases

❶ Syphilis

- Cause ⇨ Treponema pallidum (a spirochete)
- Types

  A] Congenital → abortion, IUFD, malformations (early or late)

  B] Acquired

  ↳ **1ry ⇨ hard chancre** (after 9 – 90 days)
  - Appears in LGT, anorectal region, rarely in lips
  - Painless, single (✓) or multiple firm papules → punched out ulcer
  - Painless hard non-suppurated LN
  - Infectious → spontaneously healing occurs within 6 wk

  ↳ **2ry ⇨ muco-cutaneous stage** (6 wk – 6 m)
  - General symptoms (blood spread), generalized LN
  - Rash, mucous patches esp on palms & soles
  - Condyloma latum (warty growth on vulva & perineum)
  - Infectious

  ↳ **3ry ⇨ Gumma formation**
  - Early latent (within 4 years of 2ry)
  - Late latent (> 4 yrs): Neurosyphilis or cardiovascular syphilis

- Investigations

  ☆ **Dark ground illumination in 1ry and 2ry** → spirochetes ¤

  ☆ **Non specific tests** → Wassermann, Khan, RPR, VDRL
  - . Positive after 2 weeks from chancre
  - . May be false +ve in some immune diseases such as SLE
  - . Confirm by:

  ☆ **Specific tests** → TPI, FTA

- Treatment

  Early (1ry, 2ry, 3ry < 1year)

  Benzathine penicillin 2.4 million units IM once
  Or Procaine penicillin 1 million units / day for 10 days
  Or Tetracycline / Erythromycin / Doxycycline (100 mg 1x2x14)

  Late syphilis

  Benzathine penicillin 2.4 million units IM / week for 3 wks

  Neurosyphilis

  Aqueous Penicillin G 12-24 million U/day IV for 10 days
  Then *Benzathine penicillin 2.4 million units IM* / week for 3 wks

❷ Tuberculosis

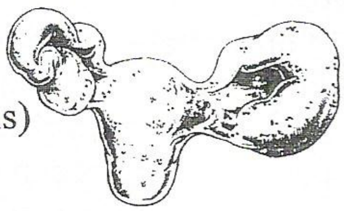
▸ **Etiology**

. Mycobacterium tuberculosis (human bacillus) > Mycobacterium bovis¤

. Becoming more common nowadays → 5% infertility cases ¤

▸ **Route of infection**

- Blood borne ✓ (from 1^{ry} pulmonary TB) → most common ¤
- Peritoneal spread (TB peritonitis)
- Lymphatic spread (TB of mesenteric LNs)
- Ascending with infected semen (TB epididymitis)



▸ **Pathology**

↳ Tubes ¤ (100%✓) ⇨ adhesive or exudative

- PERISALPINGITIS → miliary tubercles + adhesions
- INTERSTITIAL SALPINGITIS → thick, nodules, caseation
- ENDOSALPINGITIS → pyosalpinx full of caseous material
- SALPINGITIS ISTHMICA NODOSA

↳ Uterus (50%) ⇨ .Tubercles surrounded by granulomatous tissue
. Caseation, atrophy, Asherman's syndrome ¤

↳ Ovaries (25%) ⇨ may appear normal or granulomas, caseation, fibrosis

↳ Cx, vag, vulva (5%) → Hypertrophic → polypi
→ Ulcers: serpiginous outline, undermined edges, yellow floor, not indurated

▸ **Clinical picture**

↳ **History** (family or exposure or endemic area)

↳ **Symptoms**

☆ General → ±TB toxemia (NNLL)......chest symptoms of TB

☆ Abdomen → ± peritoneal TB.........ascites, sinuses

☆ Pelvic

- *Infertility* (due to ↓ GC, tubal block, anovulation, endometrial TB)
- *Pelvic congestion* ⊶
  . Pain (D's)
  . Bleeding
  . Discharge
- *Amenorrhea* (↓ GC, anovulation, endometrial TB, ↓ E by TB toxins)

↳ **Signs** General / chest
Abdominal
Local → . Tubercles (nodules) in vulva, vagina, cervix
. Uterus → ± fixed RVF
. Adenexae → ± adnexal swelling
. Douglas pouch → ± nodules

▸ Investigations

General Blood (TLC, ESR), chest X-ray

+

❶ Endometrium ($D_{\&}C$ biopsy or menstrual shedding by cx cap) for
- Zeil Neilson stain → bacilli + excess lymphocytes
- Culture on Dorset egg or Lowenstein Jensen medium
- Animal inoculation → guinea pig (liver & spleen examined after 40 days)

❷ Vulva, vagina, cervix → biopsy from lesions

❸ Tubes
* HSG → . Sausage shaped, lead pipe, hydrosalpinx, calcification ± patent
. Peritubal adhesions (localized collections of dye)
. Intrauterine adhesions, micropouche intravasations

* Endoscopy → laparoscopy + biopsy
tube is sausage shaped, pale with tubercles, calcification, caseation, dense adhesions

▸ Treatment

Medical ✓✓⇨ antituberculous drugs ¤
2 months → Isoniazid (5 mg /kg/day) +
Rifampicin (10 mg/kg/day) +
Ethambutol (15 mg/kg/day) or Streptomycin (1gm IM /day)
7 months → Rifampicin + Isoniazid

Surgical ⇨
- No tubal microsurgery (v. imp)
- TAH & BSO are only done if large masses are present ± fistula

❸ Bilharziasis

▸ Etiology → Schistosoma haematobium > Sch. Mansoni

▸ Routes of infection

Communication between *vesical*, *rectal* & *vaginal* plexus →

- Polyps ⇨ small, sessile, firm, single or multiple
- Ulcers ⇨ superficial, multiple, dirty
- Sandy patches ⇨ calcified ova beneath the surface
- Calcification ⇨ fibrosis, strictures, fistula

▸ Pathology

- ✓✓✓.....*Vulva* → pseudo-elephantiasis + thickening of hymen
- ✓✓.......*Vagina* → granular vaginitis + vaginal stenosis + polypoidal mass
- ✓.........*Cervix* → infertility
- ....*Uterus* → very rare (monthly shedding)
- ....*Tubes* → salpingitis isthmica nodosa (mucosa free i.e. tube patent)
- ....*Ovary* → large, thickened, nodular

▸ Clinical picture

History → endemic areas esp farmers

Symptoms

- Of urinary or rectal bilharziasis
- Pelvic congestion ⊶ → pain / bleeding / discharge
- Infertility (due to PID)

Signs

. Polyps / ulcers / sandy patches
. PID

▸ Investigations

- Urine & stool analysis → for ova
- Cystoscopy, sigmoidoscopy, laparoscopic biopsy
- Vulval & vaginal biopsy
- CFT

▸ Treatment

- Prophylactic
- Antibilharzial → . Biltricide (Praziquantel) single dose (20-60 mg/kg)
  . Ambilhar (niridazol) 500mg 1x3x7
- Surgical excision of residual lesions

Other organisms

❶ *Chancroid (soft sore)*

CAUSE → Haemophilus ducreyi (gram –ve bacillus)

CLINICAL PICTURE

- Papules → pustules → rupture
  ↳ soft ulcer (multiple, shallow, painful)
- Suppurative lymphadenopathy with sinus formation

INVESTIGATIONS

- *Smear* → gram stain
- *Culture* on enriched medium
- *Serology* → CFT, Fluorescent antibody
- *Biopsy*

TREATMENT………..*Tetracyclines*……..*Sulfonamides*

❷ *Granuloma inguinale*

CAUSE → Calymmato-bacterium (gram –ve bacillus)

CLINICAL PICTURE → affects vulva mainly

- Papules → rupture
  ↳ ulcers + fibrosis + stricture
- Lymphadenopathy (pseudobubo formation)

INVESTIGATION

- *Giemsa stain* → Donovan bodies (mononuclear cells containing large number of bacilli)
- *Biopsy*

TREATMENT………..*Tetracyclines*………*Erythromycin*

❸ *Actinomycosis*

ORGANISM → Actinomyces Israeli (fungus)

ROUTE OF INFECTION

- Direct spread from ruptured appendix or perforated colon → tubes
- Direct spread from rectum → vagina
- May produce PID in association with IUD

PATHOLOGY → masses, sinuses discharging pus & sulfur granules

DIAGNOSIS → Gram stain / Biopsy / Pap Smear

TREATMENT

- Remove IUCD
- Antibiotics for long time (penicillin, erythromycin, tetracycline)
- Surgery for gross pathological lesions

❹ *Human immune deficiency virus*

VIROLOGY → RNA virus (reverse transcriptase –a retrovirus–)
Destruction of T-lymphocytes → immune suppression

MODE OF INFECTION

- ☐ Sexual intercourse (semen & saliva)
- ☐ Blood or blood products / Infected syringes
- ☐ Vertical transmission (30 % of pregnancies) ❶Antepartum → placenta ❷ Intrapartum → birth canal ❸ Postpartum → lactation

CLINICAL PICTURE

1- ***Asymptomatic***...80%......................................up to 10 years
2- ***Initial HIV exposure***......fever, myalgia, generalized lymphadenopathy
3- ***Months/yrs later***.......weight loss, infections (h.zoster, oral candidiasis)
4- ***AIDS***...............Opportunistic infection → pneumonia cystitis carnii
Malignancy → Kaposi sarcoma

DIAGNOSIS

▸ **Screening for at risk population** (ELISA)
. Male homosexuals / Intravenous drug users
. Infection with other STD's / Neonates born to infected women

▸ **Confirmation**
. Western blot test
. PCR for HIV RNA (viral load)

TREATMENT

▸ **Prophylaxis**
- Avoid sexual contact with infected persons
- Proper screening for blood or its products
- Vaccination against opportunistic infections

▸ **Active**
- There is no ttt that cures HIV
- Only drugs available are to suppress viral replication
  . Retroviral inhibitors...nucleoside analogues (Zidovudine)
  . Protease inhibitor.....Indinavir
  . Fusion inhibitor.......Fuzeon
- **HAART** (**H**ighly **A**ctive **A**nti**R**etroviral **T**herapy is the combination of 2 nucleoside analogues + a protease inhibitor)
- Vaccine developm
- ent is under trial (very difficult)

Pregnancy and HIV

HIV screening should be offered for all at risk cases. Risk of fetal transfer is 15–25% (without ttt). Lactation adds another 10–15% risk while maternal ttt, CS, avoidance of breast feeding reduces that risk.